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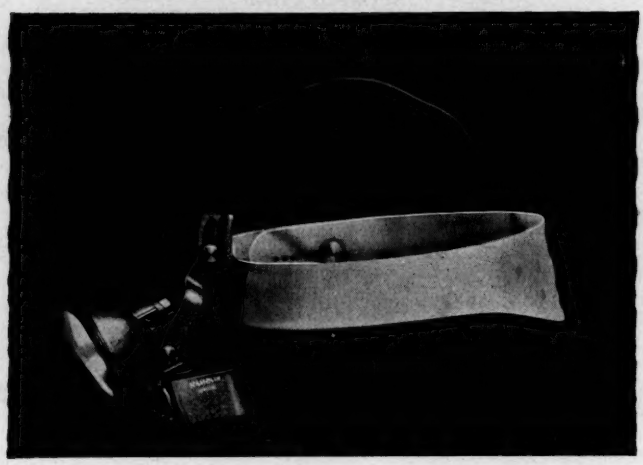

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COMMUNICATIONS

AETIOLOGY OF UVEITIS

I. DENTAL INFECTION*

BY

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FROM the beginning of the 20th century, there has been a marked tendency to ascribe uveitis to focal sepsis. There are innumerable accounts in the literature of individual cases in which uveitis has been thought to be caused in this way, the evidence usually being failure to discover any other cause or improvement in the uveitis after the sepsis is treated; in addition it is occasionally possible (Amsler, 1955) to isolate the same organism both in the aqueous humour and in a focus of infection. Against these arguments must be set the failure of treatment of focal sepsis to affect the progress of a great number of cases of uveitis, the inexplicable sudden improvement that sometimes occurs in uveitis without any relationship to such treatment (Doggart, 1951), and the failure of complete or partial treatment of focal infection to influence the frequency of relapses (Guyton and Woods, 1941).

There are also numerous surveys of series of patients with uveitis; two recent surveys give the incidence of uveitis due to focal sepsis as nil (Bennett, 1955) and 87·5 per cent. (Alvaro, 1954), and it is possible to find published series which give almost any figure between these two extremes. In assessing the value of such surveys, the methods of investigation used are of great importance, for it is obvious that some possible causes of uveitis will be missed entirely if adequate investigation is not carried out, and it is equally obvious that some possible source of focal infection will be found in the majority of patients if adequate search is made for it, though the importance ascribed to such a focus will depend on the viewpoint of the author. In addition, the type of uveitis chosen for investigation may well radically alter the relative importance of the various possible aetiologies, and any investigation which involves only a specially selected series of patients cannot give a view of the aetiology of uveitis as a whole. Judged from this point of view, the published series fail to provide any real indication of the importance of focal sepsis.

Dental infection is commonly considered to be one of the most frequent sites of focal infection associated with uveitis (Duke-Elder, 1940), the mechanism being either direct spread *via* the sinuses, focal irritation, spread

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of organisms *via* the blood stream giving rise to direct infection in the uveal tract, or an allergic reaction to bacterial products (François, 1950). Some observers have been able to induce an iritis in animals by the injection of streptococci from dental abscesses (*e.g.* Rosenow, 1915; Benedict, 1920), but the iritis is usually of a purulent nature and associated with similar lesions elsewhere in the body (Woods, 1942). Though many authors incriminate all forms of dental infection in the causation of iritis, some (*e.g.* Bedell, 1925; Cantou, 1942) believe that only closed infective lesions of the pulp or periapical tissues are responsible, parodontal infection being of no importance; Nectoux (1947), however, considered pyorrhoea to be of great importance. Some observers consider that one criterion for the definite diagnosis of an aetiological relationship with focal sepsis is that the uveitis must be of an acute serous type (Guyton and Woods, 1941).

Material and Methods

Patients with uveitis attending the Manchester Royal Eye Hospital probably form a reasonably random selection of all patients with uveitis, since it is probable that the great majority of uveitis patients from a wide area find their way to the hospital; it is fortunate in this connexion that most general practitioners make no serious attempt to treat uveitis, but refer the patient immediately to hospital, and that many patients attend the hospital without seeing their own general practitioner at all. So far as can be ascertained, there is no particular reason why the patients attending the out-patient clinic of the University Department of Ophthalmology should not form a reasonable sample of the total attending the hospital; in particular, none of the patients in this survey was referred from any of the medical or surgical departments of the Manchester Royal Infirmary who were co-operating in the investigation.

The material comprised all new patients attending the out-patient clinic of the University Department of Ophthalmology between January, 1953, and June, 1955, who were suffering from uveitis, excluding those with frankly purulent infections (panophthalmitis), post-operative uveitis, and kerato-uveitis in which the uveitis was relatively mild and apparently dependent on the accompanying keratitis (*e.g.* uveitis associated with septic corneal ulcers). Those with kerato-uveitis in which the uveitis formed a major part of the disease picture, and appeared to progress independently of the keratitis, were included in the series.

The patients were routinely referred to the Dental Department, where a complete clinical and radiological examination of the teeth was performed; almost all the patients and all the radiographs were examined by one of us (H. McI.) who was unaware of the exact type of uveitis present.

Calculation of statistical probabilities (P) was usually done by the χ^2 test, using the correction for continuity. When no value of χ^2 is given, the value of P was obtained by the exact treatment of a 2×2 Table. The level of significance observed was $P \leqslant 0{\cdot}05$.

Definition of Terms

Types of Uveitis.—The ocular disease diagnosed at the patient's first attendance was classified as kerato-uveitis, anterior uveitis (iritis or cyclitis, alone or together),

posterior uveitis (choroiditis with or without cyclitis), or pan-uveitis (iritis, cyclitis, and choroiditis). Since the diagnosis of choroiditis was made only if definite choroidal lesions were seen, some patients with lens opacities or heavy vitreous opacities diagnosed as granulomatous anterior uveitis may well have been, in fact, patients with granulomatous pan-uveitis. There is, therefore, no clear-cut distinction between these groups.

The anterior uveitis group was further sub-divided into two main types: granulomatous and non-granulomatous (Woods, 1947). Many surgeons find this classification difficult to apply in practice (e.g. Davenport, 1956), and a number of patients had to be classified as of "doubtful type".

The patients were also classified into those with and those without a definitely known association with local or general disease. Such a subdivision would possibly be made in different ways by different ophthalmologists; in the present state of our ignorance only well-substantiated causes can be accepted. We have taken uveitis to be of known association with rheumatic disease when there was either radiological evidence of spondylitis, simultaneous occurrence of the three components of Reiter's disease, or uveitis with nodular sclero-keratitis associated with rheumatoid arthritis with multiple subcutaneous nodules (Stanworth and Sharp, 1956; Stanworth, 1956). The non-rheumatic diseases associated with uveitis were considered to be herpes zoster ophthalmicus, dendritic ulceration of the cornea, interstitial keratitis, secondary syphilis, sarcoidosis, sympathetic ophthalmitis, and rupture of the lens. Superficial punctate keratitis, heterochromic cyclitis, and the Vogt-Koyanagi syndrome, though considered to be non-rheumatic (Stanworth and Sharp, 1956), were not taken to be of sufficiently definite origin to justify their inclusion, from the present point of view, in the group with a known association with local or general disease.

Types of Dental Infection.—Two conditions were considered: periapical and parodontal infections. In parodontal infection there was destruction of the alveolar bone and parodontal membrane round the tooth or teeth, associated with gingival pockets. In periapical lesions there was an area of infection surrounding the apical portion of a root or a retained root. Those retained roots which appeared to be surrounded by normal bone were classified as non-infective; they were usually roots which had been retained for many years and whose presence was unsuspected on clinical examination. Those roots which had erupted through the alveolar process were considered to be infected.

Results

Table I (overleaf) shows the numbers of patients suffering from the various types of uveitis, subdivided into those with and those without a known association with local or general disease.

The group with rheumatic disease included 29 patients with spinal arthritis (22 of whom had typical ankylosing spondylitis), nine with Reiter's disease, and one with rheumatoid arthritis.

The group with non-rheumatic disease included twelve with herpes zoster ophthalmicus, four in whom the uveitis was associated in its early stages with a dendritic corneal ulcer, two with uveitis followed by the development

TABLE I
TYPES OF UVEITIS

Association with Local or General Disease		Kerato-uveitis		Anterior Uveitis						Posterior Uveitis		Pan-uveitis		Total	
				Granulo-matous		Non-granulo-matous		Doubtful							
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Known Association	Non-rheumatic	8	7	2	2	3	1	1	—	—	—	—	—	14	10
	Rheumatic ...	—	3	1	—	23	3	5	3	—	1	—	—	29	10
	Total ...	8	10	3	2	26	4	6	3	—	1	—	—	43	20
No Known Association		8	9	11	35	32	28	12	8	9	19	2	1	74	100
Total ...		16	19	14	37	58	32	18	11	9	20	2	1	117	120

of mild interstitial keratitis due to congenital syphilis, two with secondary syphilis, two with sarcoidosis, one with uveitis due to a rupture of the lens capsule with a slow leak of lens matter, and one with sympathetic ophthalmitis.

Table II shows that dental examination was carried out in 157 of the 174 patients without known association with local or general disease, but in only 49 of the 63 patients with such association. This relatively low figure was due mainly to the fact that only 74 per cent. of the patients with rheumatic disease were dentally examined. This was because a few patients with obvious spondylitis were not referred for dental examination; the effect of the inclusion or exclusion of such patients is discussed later.

TABLE II
INCIDENCE OF PARODONTAL AND PERIAPICAL INFECTION

Association with Local or General Disease		Examined		Total with Dental Infection		Parodontal Infection		Periapical Infection	
		Male	Female	Male	Female	Male	Female	Male	Female
Known Association	Non-rheumatic	11	9	5	5	3	5	3	1
	Rheumatic ...	23	6	8	3	6	2	4	1
	Total ...	34	15	13	8	9	7	7	2
No Known Association ...		67	90	27	33	24	21	8	16
Total ...		101	105	40	41	33	28	15	18

Table II also shows that there was no significant difference in the incidence of dental infection in males and females, or in those with and without a

significant association with local or general disease; this was in accordance with the impression received during the clinical examinations that the incidence of dental disease was much the same as that in the general hospital population. The incidence of dental infection in uveitis associated with rheumatism was the same as in the whole series, and was independent of whether or not they were aware of their rheumatic disease (Table III), except perhaps for periapical infection in the age group under 41 years. This does not suggest that these patients had had any special treatment for dental infection because of their rheumatism, and, so far as parodontal infection is concerned, there is no need to eliminate them from the series. No special dental treatment had been given to any of the patients with uveitis associated with non-rheumatic disease. The incidence of dental infection (17 in 52 patients examined) in those patients who had had previous attacks of uveitis was not significantly less than that in the whole series.

TABLE III
DENTAL INFECTION IN RHEUMATIC DISEASE

Rheumatic Disease	Age (yrs)	No. of Patients	Number Examined	Total with Dental Infection	Par-odontal Infection	Periapical Infection
Known to Patient ...	<41	14	11	3	3	1
	>40	13	8	5	3	2
	Total	27	19	8	6	3
Not Known to Patient ...	<41	8	6	3	1	2
	>40	4	4	1	1	—
	Total	12	10	4	2	2

The distribution of dental infection among the varieties of uveitis is shown in Table IV.

TABLE IV
DENTAL INFECTION IN VARIETIES OF UVEITIS

Association with Local or General Disease		Kerato-uveitis	Anterior Uveitis			Posterior Uveitis	Pan-uveitis	Total
			Granulo-matous	Non-granulo-matous	Doubtful Type			
Known Association	Examined	16	5	21	6	1	—	49
	Total with Dental Infection	10	1	9	2	—	—	22
	Parodontal Infection	8	1	6	1	—	—	16
	Periapical Infection	4	—	4	1	—	—	9
No Known Association	Examined	15	40	58	14	27	3	157
	Total with Dental Infection	4	17	20	3	13	2	59
	Parodontal Infection	2	15	16	2	8	2	45
	Periapical Infection	3	6	6	2	7	—	24

There was a slight tendency for parodontal infection to be associated with granulomatous anterior uveitis in the group of unknown aetiology, and for root infection to be associated with posterior uveitis, but neither of these tendencies was statistically significant.

Since the incidence of dental infection varies with age, it was studied in patients aged less than 21 years, 21–40 years, 41–50 years, and more than 50 years. There was no appreciable difference in the incidence of parodontal disease in the various types of uveitis in patients of any age group except 21–40 years, in which (Table V) there was a marked tendency for parodontal infection to occur in patients with granulomatous anterior uveitis of no known association; the difference in incidence between this group (67 per cent.) and the remainder of the series (32 per cent.) was significant ($P = 0{\cdot}03$). The exclusion of patients who had had previous attacks of uveitis left the level of significance unchanged.

TABLE V

DENTAL INFECTION, AGE GROUP 21–40 YEARS

Association with Local or General Disease		Kerato-uveitis	Anterior Uveitis			Posterior Uveitis	Pan-uveitis	Total
			Granulomatous	Non-granulomatous	Doubtful Type			
Known Association	Examined	3	—	14	1	1	—	19
	Total with Dental Infection... ...	3	—	5	—	—	—	8
	Parodontal Infection	3	—	3	—	—	—	6
	Periapical Infection	1	—	3	—	—	—	4
No Known Association	Examined	4	12	17	6	13	—	52
	Total with Dental Infection... ...	2	9	7	2	9	—	29
	Parodontal Infection	1	8	5	1	6	—	21
	Periapical Infection	2	4	2	1	5	—	14

It has already been pointed out that the diagnosis of the granulomatous nature of the uveitis was not always easy, so that the classification of individual patients might vary a little with different ophthalmic surgeons. It was possible, however, to subdivide the patients with granulomatous anterior uveitis into two sub-groups: those in whom the uveitis was of an obvious chronic and granulomatous type, and those in whom these features were not so marked (Table VI, opposite). It will be seen that the incidence of parodontal infection was obviously greater in the very chronic type; if we compare the incidence in this type in the age group 21–40 years (six out of seven patients), with the incidence in the remainder of the age group (21 out of 64 patients) the difference is statistically significant ($P = 0{\cdot}01$). The

parodontal infection was generalized in three of these six patients, and there was no tendency to involve particularly the upper jaw or the mouth on the same side as the eye lesion; the infection in these patients appeared to be more generalized than in those patients with the less chronic type of uveitis.

TABLE VI
DENTAL INFECTION IN GRANULOMATOUS ANTERIOR UVEITIS OF UNKNOWN AETIOLOGY

Age Group		Chronic Type	Less Chronic Type	Total
All Ages	No. of Patients	26	20	46
	No. Examined	23	17	40
	Parodontal Infection	10	5	15
Age 21–40	No. of Patients	7	6	13
	No. Examined	7	5	12
	Parodontal Infection	6	2	8

It is possible that parodontal infection may also have been associated with pan-uveitis, since two of the three such patients were found to have parodontal infection, and there is no clear-cut difference in this series between granulomatous anterior uveitis and pan-uveitis.

The incidence of parodontal infection was higher (38 per cent.) in the age groups 21–40 years than in the other age groups (25 per cent.), presumably largely because the dental state of younger people is usually good, and because in older patients parodontal sepsis tends to clear up as the teeth are lost. This may be responsible for the fact that the incidence of such infection was significant only in this age group; in other age groups, individual patients may have had uveitis genuinely associated with parodontal disease, but for most patients other factors must have been predominant.

There was a tendency in patients aged 21–40 years for there to be an increased incidence (38 per cent.) of root infection in posterior uveitis of unknown origin compared with that in the remainder of the series (22 per cent.) or in uveitis associated with local or general disease (21 per cent.). Root infection was, however, less common in those patients under the age of 41 years with rheumatic diseases of which they were aware (Table III) and, when these patients were eliminated, the incidence in patients other than those with posterior uveitis of unknown origin rose to 25 per cent. (12 patients in 47) and in patients with uveitis associated with local or general disease to 37 per cent. (three patients in eight), so that the incidence in posterior uveitis was obviously not statistically significant.

II. UPPER RESPIRATORY TRACT AND OTHER INFECTIONS

BY

A. STANWORTH

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THE tonsils are often considered (Duke-Elder, 1940) to be, with the teeth, the main source of focal infection responsible for uveitis, nasal sinus infection being thought to be of less importance. The significant organisms concerned are usually thought to be the various types of streptococci, and Woods (1950, 1953, 1956a) has made the most comprehensive study of the relationship; he found a much higher incidence (85 per cent.) of skin hypersensitivity to streptococcal vaccines among patients with non-granulomatous uveitis than among those with granulomatous uveitis (27 per cent.); the incidence of foci of infection was 54 and 30 per cent. respectively. The results of treatment by desensitization appeared to be good. These findings are in accordance with Wood's view that the clinical appearance and histological changes in granulomatous anterior uveitis indicate a chronically infected uveal tract, whereas those in non-granulomatous uveitis are similar to the allergic focal reactions produced in tuberculous eyes by the systemic administration of excessive amounts of tuberculin. Alvaro (1954) found that cutaneous sensitivity tests for streptococci were entirely negative in only one of 97 patients with uveitis, and ascribed uveitis to focal sepsis in 87 per cent. of patients.

As with all types of focal infection, one of the main difficulties is the frequency of upper respiratory tract infections in patients without uveitis. Apart from the skin tests already mentioned, two methods have been suggested for identifying those patients in whom the focal infection is causally related to uveitis. Harley (1952), believing that skin sensitivity reactions bore little relationship to uveal sensitivity, preferred the "pathogen selective culture", the principle of which is the "utilization of the *in vitro* bactericidal power of the patient's whole fresh blood to kill off organisms to which he is immune and to allow the growth of potentially pathogenic organisms, thus assisting us to select the aetiologically important organisms from a mixed culture". Dekking (1954) studied the antistreptolysin titre (A.S.T.) and agglutination tests to O- and L-agglutinins in the patient's serum; he considered that there was a relation between these and uveitis if certain combinations were present, namely L and O positive; high A.S.T. and L and O; A.S.T. and O, or high L. High A.S.Ts. in uveitis were also found by Schöne and Steen (1951) and Smith and Ashton (1955), and, together with raised streptococcal anti-hyaluronidase titres, by Leopold and Dickinson (1954). Otten and Westendorp Boerma (1954), however, found that the A.S.Ts. and L- and O-agglutination titres were raised, not only in rheumatoid arthritis, but also in many internal diseases, such as carcinoma, hepatitis, jaundice, ulcers of the digestive tract, heart failure, and diabetes, none of which was

associated with clinical streptococcal infection; Vesterdal (1951) found the A.S.T. to be of little value; and after further experience Hallett, Leopold, and Inwald (1956) found that streptococcal anti-hyaluronidase titres were normal in uveitis.

Material and Methods

The patients concerned, and the classification of the uveitis present, have already been described in the first paper in this series (Stanworth and McIntyre, 1957).

The patients were routinely referred for radiographs of the nasal sinuses, and those who showed any radiographic changes were referred to an Ear, Nose, and Throat surgeon for further investigation. Direct cultures were taken from the nasal vestibule and the throat, and the pathogen selective culture was also carried out on the throat swabs.

Results

Nasal Sinus Infections.—The incidence of radiographic sinus changes is shown in Table VII; there was a tendency, not quite statistically significant ($\chi^2 = 3{\cdot}5$; $P = 0{\cdot}06$) for there to be a greater incidence in males than in females, but this was present in the patients with a significant association with local or general disease as well as in those without, and there was no tendency for an increased incidence in all the patients with uveitis of unknown aetiology.

TABLE VII

INCIDENCE OF RADIOGRAPHIC CHANGES IN NASAL SINUSES

Association with Local or General Disease		Male		Female		Total	
		Radiographs Taken	No. Positive	Radiographs Taken	No. Positive	Radiographs Taken	No. Positive
Known Association	Non-rheumatic ...	11	6	8	2	19	8
	Rheumatic ...	25	9	7	1	32	10
	Total	36	15	15	3	51	18
No Known Association ...		66	22	94	22	160	44
Total		102	37	109	25	211	62

The incidence of radiographic changes was almost as great in those rheumatic patients who were aware of their disease (six out of twenty radiographs) as in those who were not aware of it (four out of twelve radiographs) and was the same as in the series as a whole; the incidence in patients who had had previous attacks of uveitis (nineteen in 54 patients) was also as great as in the whole series; there was, then, no evidence that these patients had had special treatment for sinus infection.

The distribution of radiographic changes among the varieties of uveitis is shown in Table VIII (overleaf); there was no significantly increased incidence in any variety. Of the 62 patients with radiographic changes, 37 were seen by the E.N.T. surgeon; the incidence of clinical sinus infection is shown in

Table VIII. The incidence in those patients examined by the E.N.T. surgeon was higher in granulomatous anterior uveitis of unknown association (78 per cent.) than in the remainder of the series (36 per cent.); this difference was just significant ($P = 0{\cdot}04$). The proportion of patients with radiographic changes who attended for clinical examination (60 per cent.) was unfortunately rather low, though it was the same for granulomatous anterior uveitis of unknown association as for the series as a whole.

TABLE VIII

SINUS CHANGES IN VARIETIES OF UVEITIS

Association with Local or General Disease		Kerato-uveitis	Anterior Uveitis			Posterior Uveitis	Pan-uveitis	Total
			Granulo-matous	Non-Granulo-matous	Doubtful Type			
Known Association	Radiographs Taken	14	4	25	7	1	—	51
	No. Positive ...	6	1	9	2	—	—	18
	E.N.T. Examination	4	—	4	1	—	—	9
	Clinical Infection	2	—	2	1	—	—	5
No Known Association	Radiographs Taken	16	43	54	17	27	3	160
	No. Positive	5	14	11	7	6	1	44
	E.N.T. Examination	4	9	4	5	5	1	28
	Clinical Infection	1	7	—	2	2	—	12

Eleven patients with granulomatous anterior uveitis of unknown association, aged over 50 years, had radiographic sinus changes; seven of them were examined clinically, six (86 per cent.) being found to have sinus infection. In the remaining varieties of uveitis, fourteen patients were in the same age group; nine were examined clinically, but only two (22 per cent.) showed sinus infection; the difference in percentage is significant ($P = 0{\cdot}02$).

If we consider the patients who were fully investigated for sinus infection (i.e. were shown to be without radiographic changes, or, having such changes, were seen by the E.N.T. surgeon), the group with granulomatous anterior uveitis of unknown association contained 18 per cent. (seven of 38 patients) with clinical infection, compared with 7 per cent. (ten of 148 patients) in the remainder of the series; this difference is not quite significant by the χ^2 test ($\chi^2 = 3{\cdot}7$; $P = 0{\cdot}06$), though this test is not very accurate with these small numbers. In females, five of 29 patients with granulomatous anterior uveitis of no known association had clinical sinus infection, compared with three of 72 patients in the remainder of the series; this difference is just significant ($P = 0{\cdot}04$). In patients over 50 years of age, 33 per cent. (six of eighteen patients) with granulomatous anterior uveitis of no known association showed clinical infection, compared with 4 per cent. (two of 47 patients) in the remainder of the series; this difference is highly significant ($P = 0{\cdot}005$);

only four females in this age group had clinical sinus infection, and all had granulomatous anterior uveitis.

The very chronic type of granulomatous anterior uveitis of unknown association is compared with the less chronic type in Table IX.

There is a tendency, not statistically significant, for the very chronic type to be associated with a greater proportion of positive radiographs and of clinical sinus infection.

TABLE IX

NASAL SINUS INFECTION IN GRANULOMATOUS ANTERIOR UVEITIS OF UNKNOWN ASSOCIATION

Age Group (yrs)		Chronic Type		Less Chronic Type		Total	
		Male	Female	Male	Female	Male	Female
All Ages	No. of Patients ...	4	22	7	13	11	35
	Radiographs Taken ...	4	21	7	11	11	32
	No. Positive	2	9	2	1	4	10
	E.N.T. Examination...	2	6	—	1	2	7
	Clinical Infection ...	2	4	—	1	2	5
>50	No. of Patients ...	2	12	4	7	6	19
	Radiographs Taken ...	2	11	4	5	6	16
	No. Positive ...	2	6	2	1	4	7
	E.N.T. Examination...	2	4	—	1	2	5
	Clinical Infection ...	2	2	—	1	2	4

The increased incidence of clinical sinus infection in granulomatous anterior uveitis in patients over the age of 50 years is complementary to the increased incidence of dental infection already found in the age group 21–40 years. In patients of all ages who were investigated fully for both dental and sinus infections, 50 per cent. (eighteen of 36 patients) of cases of this variety of uveitis showed one or both infections, compared with 27 per cent. (38 of 140 patients) of the remainder of the series; this difference is significant ($\chi^2 = 6{\cdot}0$; $P < 0{\cdot}02$).

Throat Cultures.—The organisms of greatest interest are those which are not normally found in the upper respiratory tract, particularly *Streptococcus haemolyticus*. *Streptococcus viridans* is a normal finding in throat cultures, and was only noted when it was obviously the preponderating organism present. The other organisms noted were pneumococcus, *Streptococcus faecalis*, non-haemolytic streptococcus, and *Haemophilus influenzae* and *para-influenzae*.

The incidence of positive direct throat cultures is shown in Table X (overleaf); there was an increased incidence of *Streptococcus haemolyticus* in the group of uveitis with no known association, especially in anterior uveitis, but this was not statistically significant.

TABLE X
ROUTINE THROAT CULTURES

Association with Local or General Disease		Kerato-uveitis	Anterior Uveitis			Posterior Uveitis	Pan-uveitis	Total
			Granulo-matous	Non-Granulo-matous	Doubtful Type			
Known Association	Cultures Taken ...	12	5	24	6	—	—	47
	Strep. haemolyticus	—	—	2	—	—	—	2
	Strep. viridans ...	2	1	3	2	—	—	8
	Others	—	1	1	1	—	—	3
No Known Association	Cultures Taken ...	16	45	59	16	26	3	165
	Strep. haemolyticus	3	9	11	1	3	—	27
	Strep. viridans ...	4	12	11	3	10	1	41
	Others	3	5	5	—	—	—	13

Pathogen selective cultures were taken from 184 patients; only 21 failed to grow *Streptococcus viridans*, and only nine of these failed to grow either *Streptococcus haemolyticus* or one of the other organisms listed above, and the cultures from patients with known association with local or general disease did not behave differently from the remainder of the series. Of the 42 pathogen selective cultures from patients with *Streptococcus viridans* predominating in their direct throat cultures, 36 grew this organism, including five of the six from patients with known association with local or general disease; fifteen of the 28 pathogen selective cultures from patients with *Streptococcus haemolyticus* in the direct throat cultures grew this organism, including the cultures from each of the two patients with a known association with local or general disease, one having secondary syphilis and one typical ankylosing spondylitis. It is obvious, therefore, that the pathogen selective test does not predict which organisms are related to the uveitis.

Streptococcus haemolyticus was grown in the pathogen selective cultures of four patients in whom direct throat cultures had failed to reveal it, two having non-granulomatous anterior uveitis, one granulomatous anterior uveitis, and one posterior uveitis, all without known association with local or general disease. Dr. F. B. Jackson (personal communication), who carried out these cultures, considers that " these were certainly not due to contamination, or to a bacteriaemia, but were probably present in the secretion from the patients, being overgrown by the normal upper respiratory tract flora (in spite of the use of selective media), but growing when large proportions of the normal flora were inhibited, as appeared to be the case when cultures from the throat were incubated in the presence of the patient's blood ". The method may therefore possibly be of help in isolating *Streptococcus haemolyticus*; the almost universal presence of *Streptococcus viridans* in the

pathogen selective culture indicates that the latter is of no value as far as this organism is concerned.

Nasal Cultures.—These were taken from 207 patients; only two showed *Streptococcus haemolyticus*, both being from patients with anterior uveitis of no known association, one granulomatous and one non-granulomatous; the latter also had *Streptococcus haemolyticus* in the throat culture. There was no suggestion of a significant incidence of *Streptococcus viridans* infection.

Combined Nose and Throat Cultures

Streptococcus haemolyticus.—The incidence of *Streptococcus haemolyticus* in those patients who have had all three investigations performed (nasal, direct throat, and pathogen selective cultures) is shown in Table XI.

The incidence of positive cultures in patients with rheumatic disease was low; seventeen patients who were aware of their rheumatic disease had all the cultures performed, none being positive for *Streptococcus haemolyticus*; if these patients were eliminated, the increased incidence of positive cultures in uveitis of no known association is not significant. In these patients, the incidence in those with previous attacks of uveitis (seven in 38 patients) was almost the same as in those without previous attacks (26 in 124 patients).

TABLE XI

COMBINED NOSE AND THROAT CULTURE

Association with Local or General Disease		Male			Female			Total		
		No. of Patients	*Strep. haemolyticus*	Pneumo-coccus	No. of Patients	*Strep. haemolyticus*	Pneumo-coccus	No. of Patients	*Strep. haemolyticus*	Pneumo-coccus
Known Association	Non-rheumatic ...	7	1	1	5	—	1	12	1	2
	Rheumatic ...	21	1	—	5	—	1	26	1	1
	Total	28	2	1	10	—	2	38	2	3
No Known Association ...		63	9	9	78	22	9	141	31	18
Total		91	11	10	88	22	11	179	33	21

The distribution of positive cultures in the varieties of uveitis is shown in Table XII (overleaf), which does not include patients with rheumatic disease of which they were aware. The increased incidence in the patients with no known association with local or general disease occurred mainly in those with anterior uveitis, but the difference between this group and the remainder of the series was not statistically significant.

In patients aged over 40 years, there was an increased incidence in patients with anterior uveitis without known association with local or general disease

(twenty positive cultures in seventy patients) compared with the remainder of the series (two in 29 patients); this difference is significant ($\chi^2 = 4{\cdot}4$, $P = 0{\cdot}04$). In the age group 41–50 years, the incidence in granulomatous anterior uveitis (57 per cent.) was greater than in the remainder of the anterior uveitis group (36 per cent.), and this was even more marked in patients aged over 50 years (30 and 6 per cent. respectively). In the latter age group, the incidence in granulomatous anterior uveitis (six in twenty patients) was significantly higher ($P < 0{\cdot}01$) than in the remainder of the series (one in 33 patients); the increased incidence appeared to be independent of sex. The incidence of positive cultures in granulomatous anterior uveitis was greater in the chronic type (38 per cent.) than in the less chronic type (18 per cent.). The proportion of positive cultures in granulomatous anterior uveitis was consistently high throughout the year, so the association was not due to a tendency for patients with this type of uveitis to attend at a time when *Streptococcus haemolyticus* was common.

The association of *Streptococcus haemolyticus* with granulomatous anterior uveitis becomes clearer if one considers the relationship of positive cultures to clinical sepsis in the teeth and nasal sinuses. It is not unreasonable to assume that patients with such sepsis may have a greater tendency to harbour streptococci in nose and throat, and that this may bear little relationship to uveitis in those patients. In patients who were fully investigated both for sepsis and for *Streptococcus haemolyticus*, the total incidence of positive cultures in patients with parodontal or sinus sepsis (eleven in 42 patients) was indeed higher than that in patients without sepsis (eighteen in ninety patients), and it did not show any tendency to be greater in patients with anterior uveitis of no known association; in patients without sepsis, however, the incidence was obviously much higher (seven in fourteen patients) in patients with granulomatous anterior uveitis than in the remainder of the series (eleven in 76 patients); the χ^2 test shows this to be significant ($\chi^2 = 7{\cdot}3$; $P < 0{\cdot}01$), though with these relatively small numbers the level of significance is not given accurately. In females without clinical sepsis, six of eleven patients with granulomatous anterior uveitis of no known association had positive cultures, compared with eight of forty in the remainder of the series; this difference is significant ($P = 0{\cdot}03$).

In all cases, the organism was tested to see whether or not it belonged to Lancefield groups A, B, C, D, or G. In granulomatous anterior uveitis, a Group-A streptococcus was found in only one patient, who had a strongly positive gonococcal complement-fixation test and radiological evidence of active chest tuberculosis; a Group-C streptococcus was found in one patient, and a streptococcus belonging to none of the above groups in the remaining nine patients. In the remainder of the series, the organism belonged to Group A in three patients, to Groups B, C, and D in one patient each, to Group G in four patients, and to none of the above groups in thirteen patients.

Streptococcus viridans.—It has already been pointed out that the almost universal presence of *Streptococcus viridans* in the pathogen selective cultures makes this test useless for this organism. In those patients who had both nasal and direct throat cultures performed, there was no evidence of increased incidence in any type of uveitis in any age group.

Pneumococci.—These were cultured from 23 patients, 21 of whom had had all three cultures performed (Table XI). In the series as a whole, there was no significantly increased incidence in any variety of uveitis (Table XII), but in patients aged less than 41 years, there was a higher incidence in those with anterior uveitis of no known association (nine in 32 patients) than in the remainder of the age group (one in 31 patients); the difference was statistically significant ($P<0{\cdot}01$). In this age group, both males and females showed a high incidence; there was no evidence that seasonal factors played a part.

TABLE XII

NOSE AND THROAT CULTURES: VARIETIES OF UVEITIS

Association with Local or General Disease*		Kerato-uveitis	Anterior Uveitis			Posterior Uveitis	Pan-uveitis	Total
			Granulo-matous	Non-Granulo-matous	Doubtful Type			
Known Association	No. of patients ...	7	3	9	2	—	—	21
	Strep. haemolyticus	—	—	2	—	—	—	2
	Pneumococcus ...	—	1	1	1	—	—	3
No Known Association	No. of Patients ...	15	38	50	14	22	2	141
	Strep. haemolyticus	3	11	13	1	3	—	31
	Pneumococcus ...	2	7	8	1	—	—	18

* Patients aware of their rheumatic disease are excluded

In patients who had been fully investigated for dental and sinus sepsis and for pneumococcal infection, the total incidence of positive cultures was almost the same in those with sepsis as in those without; in both groups it was higher in those with anterior uveitis of no known association than in the remainder, but in neither group was the difference statistically significant. In patients under the age of 41 years without clinical parodontal or nasal sinus sepsis, six of the fourteen patients with anterior uveitis of no known association had positive cultures, compared with none of the fifteen patients in the remainder of the series; this difference is significant ($P<0{\cdot}01$). Positive cultures were found in both the patients with uveitis of granulomatous type and in three of the eight patients with uveitis of non-granulomatous type.

Seven patients with granulomatous anterior uveitis of no known association, only two of whom were aged less than 41 years, were found to be free from parodontal, sinus, and *Streptococcus haemolyticus* infections after full

investigation; three of them had pneumococcal infection; this incidence is just significant ($P = 0{\cdot}048$) when compared with that in all patients who were fully investigated (excluding those who were aware of their rheumatic disease). This suggests that the association of pneumococcal infection with anterior uveitis was primarily with the granulomatous type. There were, however, seven more patients with granulomatous anterior uveitis who had full investigation of their nose and throat cultures, but who did not have either their teeth or sinuses fully examined; none of these patients had pneumococci in their cultures, and although only one of these patients was under 40 years of age, this throws some doubt on the possibility that there is a particular association between pneumococci and granulomatous anterior uveitis.

Other Organisms.—Streptococcus faecalis was cultured in four patients, and non-haemolytic streptococci in three; in each case, one patient had uveitis associated with rheumatic disease, so that there was no evidence of a significant association of these organisms with uveitis. *Haemophilus influenzae* or *para-influenzae* was cultured in seven patients; two had kerato-uveitis, one granulomatous anterior uveitis, two non-granulomatous anterior uveitis, and two anterior uveitis of a doubtful type, all with no known association with local or general disease. *Bacillus proteus* was cultured in one patient with granulomatous anterior uveitis of no known association.

Other Infections.—Particular interest centres in those patients with granulomatous anterior uveitis who did not show sepsis in teeth or sinuses or infection with *Streptococcus haemolyticus.*

There were seven such patients among those who were fully investigated for infection.

Three of these had pneumococcal infection, one also having chronic generalized gingivitis (which had not been considered sufficient to justify a diagnosis of par-odontal infection) together with some bone absorption around $\underline{7}|$; he also gave a history of in-patient treatment for maxillary sinusitis in 1951.

One patient showed *Bacillus proteus* in the throat.

Two other patients had no evidence whatsoever of infection.

The seventh patient (**Case 1**), a female aged 41 years, had chronic asthma and eczema; the urine showed albumin, pus, and red blood cells, and the gonococcal complement-fixation test, carried out on three occasions, was positive once and doubtful twice. The venereologist thought it was extremely doubtful if the aetiology were gonococcal. The full blood count was borderline, showing 11,000 white cells (71 per cent. polymorphs); a second count showed 10,800 white cells (67 per cent. polymorphs). Rheumatological examination was negative, but radiographs were not taken.

In addition to this patient, genito-urinary infection was proved in two others (Cases 2 and 3) with granulomatous anterior uveitis.

Case 2, a female aged 48 years, had leucorrhoea, probably due to *Trichomonas vaginalis,* and chronic cervicitis; a catheter specimen of urine showed pus and red blood cells, but culture was sterile; throat swab showed haemolytic streptococci and *B. coli,* and swabs from an ulcerated nipple showed pneumococci.

Case 3, a female aged 76 years, had cystitis due to infection with *Bacillus coli.*

On the other hand, one patient with uveitis associated with dendritic corneal ulceration also had cystitis due to *Bacillus coli* infection, and one patient (Case 13) with anterior uveitis of doubtful type had albuminuria, diabetes, and uraemia, from which he died; no *post mortem* examination was carried out.

Four other patients, none of whom had granulomatous anterior uveitis, had albuminuria on their first examination, but a second examination in three of them was normal; the fourth did not attend for further examination. It may be, therefore, that the association of granulomatous anterior uveitis with genito-urinary infection in the cases described above was coincidental.

One of the patients with genito-urinary infection and granulomatous uveitis (Case 3) also had radiographic evidence of marked bronchitic changes in both lung fields; in addition, one patient with kerato-uveitis had radiographic and clinical evidence of bronchiectasis. One patient with non-granulomatous anterior uveitis and definite ankylosing spondylitis gave a history of pneumonia 3 weeks before the onset of uveitis, but this was shown to be associated with a bronchogenic carcinoma. A history of recent bronchitis or influenza was given by five other patients, two having non-granulomatous anterior uveitis, one anterior uveitis of doubtful type, one posterior uveitis, and one kerato-uveitis; in all cases there were no recent radiographic lung changes. Four patients had chronic bronchitis without radiographic changes; one had granulomatous anterior uveitis associated with nasal sinus and *Streptococcus haemolyticus* infections, one had posterior uveitis, and two had non-granulomatous anterior uveitis, including one with ankylosing spondylitis. There is, therefore, no evidence of a special relationship between influenza or bronchitis and any particular type of uveitis.

One patient with posterior uveitis gave a history of recent tonsillitis, but cultures showed no significant organisms; and one patient had kerato-uveitis and chronic osteomyelitis of the elbow with a discharging sinus due to a war injury.

A full blood count was performed on 208 patients; the upper limit of white cells was taken to be 11,000, with up to 70 per cent. polymorphs (or up to 7,500 polymorphs per cu. mm.). On this basis, 21 patients had polymorpho-leucocytosis; of these, eighteen had one or more infections of the teeth, nasal sinuses, or throat, one had radiographic neoplastic changes in the pelvis and spine, one was pregnant, and one had typical ankylosing spondylitis and had not been examined by the dental surgeon.

There was, therefore, no definite evidence of significant infections other than those in the teeth and upper respiratory tract.

Incidence of Significant Focal Infection

In patients who have had a full investigation for parodontal, nasal sinus, and *Streptococcus haemolyticus* infections, excluding those with rheumatic disease of which they were aware, 23 (77 per cent.) of the thirty patients with granulomatous anterior uveitis of otherwise unknown association had proved infection, compared with 37 (36 per cent.) of the remaining 102 patients in the series; this difference is highly significant ($\chi^2 = 13{\cdot}5$; $P < 0{\cdot}001$).

Included in these thirty patients with granulomatous anterior uveitis were

two with heterochromic cyclitis and one with the Vogt-Koyanagi syndrome, all of whom had one of the forms of infection. If it is assumed that these diseases were not associated with infection except by chance, twenty of the remaining 27 patients had infection, compared with forty of the 105 patients in the remainder of the series; the difference is still highly significant ($\chi^2 = 9{\cdot}8$; $P = 0{\cdot}01$). Infection was found in only three of the 23 patients in the remainder of the series who had had previous attacks; even when these patients are excluded, the increased incidence in granulomatous anterior uveitis was still significant ($\chi^2 = 5{\cdot}7$; $P = 0{\cdot}02$).

Eighteen of the 26 patients with granulomatous anterior uveitis of the very chronic type had proved infection, including fifteen of the seventeen who were fully investigated for these infections. Alternatively the patients with granulomatous anterior uveitis may be subdivided into those in whom pan-uveitis could or could not be excluded; of the latter, sixteen of seventeen patients who were fully investigated had proved infection, compared with seven of thirteen in whom pan-uveitis could be excluded. Both the patients with pan-uveitis who had been fully investigated had proved infection.

Patients with granulomatous anterior uveitis or pan-uveitis and parodontal, nasal sinus, or *Streptococcus haemolyticus* infection will therefore be considered as a separate group in which uveitis was "associated with infection". This comprised one patient with sarcoidosis and 28 patients with uveitis of hitherto unknown association, including two patients with heterochromic cyclitis, one with the Vogt-Koyanagi syndrome, one with probably active chest tubercle, and one with inadequately treated congenital syphilis. Since parodontal, sinus, and haemolytic streptococcal infections are relatively common, it must be expected that the association in some of these patients was due to coincidence.

The importance of the association of anterior uveitis with pneumococcal infection in the nose and throat is more difficult to evaluate. It was not certain that the association was with the granulomatous type of anterior uveitis, and it was apparently confined, for no very obvious reason, to patients under the age of 41 years.

Focal Infection as a Cause of Uveitis

The finding of an association of uveitis with infection does not in itself, of course, necessarily indicate that the connexion is a causal one. It may well be that patients with granulomatous uveitis due to some unknown cause are also liable to infections. If this were the case, it might be expected that the same type of uveitis might show an increased tendency to be associated with other infections; this was not found to be the case, except possibly for infection with the pneumococcus, which can in any case be considered to be a form of streptococcus.

If the infection is of causal significance, it would be expected that treat-

ment of the infection would lead to an improvement in the prognosis for the ocular disease. This was not found to be the case by Guyton and Woods (1941); they were, however, studying mainly the incidence of recurrences in non-granulomatous uveitis. In the present series it was not considered justifiable, in the present state of our knowledge, to withhold treatment for any septic process discovered in the teeth or sinuses, and the only patients who did not receive such treatment were therefore those who defaulted. No attempt was made, however, to eliminate *Streptococcus haemolyticus* from the nose or throat, so a comparison may be made (Table XIII) between those in whom the infection (*i.e.* parodontal or sinus infection) was adequately treated, and those in whom the infection (*i.e. Streptococcus haemolyticus* infection with or without parodontal or sinus infection) was untreated or incompletely treated. The criterion of resolution of the uveitis was the cessation of all treatment with mydriatics. The period of follow-up varied from 1 to 3½ years (average 2½ years) and was the same for the two groups. Table XIII shows that the prognosis for patients with infection was better for those adequately treated; treatment of parodontal or sinus infection in those patients in whom *Streptococcus haemolyticus* was also found gave no better prognosis than in those patients with streptococci alone. The prognosis was intermediate in those patients in whom no infection was found. These findings were consistent with an association between adequate treatment of the infection and an improvement in the ocular prognosis, but they may also be interpreted as indicating merely that uveitis associated with *Streptococcus haemolyticus* infection had inherently a worse prognosis than uveitis associated with parodontal or sinus infection.

TABLE XIII

GRANULOMATOUS ANTERIOR UVEITIS AND PAN-UVEITIS: RESPONSE TO TREATMENT OF INFECTION

Type of Patient	Treatment of Infection	Total Followed-up	Resolved in		Still under Treatment	Recurrence after Resolution	Unsatisfactory Response	
			6 Months or Less	More than 6 Months			Total	Percentage
All Patients	No Infection Found ...	18	13	1	4	3	7	39
	Adequately Treated ...	14	9	2	3	—	3	21
	Not adequately Treated	10	5	2	3	3	6	60
No. fully Investigated for Infection	No Infection Found ...	7	5	1	1	1	2	29
	Adequately Treated ...	11	7	2	2	—	2	18
	Not adequately Treated	10	5	2	3	3	6	60

If sepsis were the sole cause of the uveitis in these patients, it would be expected that adequate treatment would, in all cases, lead to a resolution

of the ocular inflammation; the histories of the three patients (Cases 4, 5, and 6) who had an unsatisfactory response are therefore of interest; all had granulomatous anterior uveitis in which pan-uveitis could not be excluded, and in two (Cases 4 and 6) the uveitis was of the very chronic type.

Case 4, a male aged 35 years, had been treated elsewhere for 5 weeks; his visual acuity when first seen was hand movements only. The only significant finding on investigation was a discharging parodontal abscess, which was treated by removal of carious teeth. In spite of local treatment, combined at various times with systemic cortisone and protein shock therapy, the eye, though much less actively inflamed, was still under treatment 18 months later at the time of the follow-up survey, but 3 months after this treatment was discontinued, the eye being quiet and without keratic precipitates, but soft and becoming divergent.

Case 5, a female aged 43 years, had had treatment intermittently elsewhere for 16 months, and when first seen had secondary glaucoma, for which a trephine operation was performed. The only significant finding on investigation was parodontal disease of the lower anteriors, with radiological evidence of loss of alveolar bone. She was still under treatment 12 months later at the time of the follow-up survey, but the keratic precipitates, dilated iris vessels, and vascular exudate in the pupillary area were slowly subsiding; local treatment was discontinued 3 months later, and the patient is being fitted with a cosmetic contact lens.

Case 6, a female aged 59 years, had had bilateral iridectomy elsewhere for chronic cyclitis 9 months previously, and the inflammation had become active again 2 months before she attended the University Department; the visual acuity was less than 6/60. The only significant findings on investigation were chronic parodontal and nasal sinus infections, which were successfully treated by dental extractions and antral lavage; a nasal culture had not been taken. In spite of local treatment and protein shock therapy, the cyclitis still showed periodic evidence of activity at the time of the follow-up survey 18 months later; a nasal culture, taken to complete the full investigation for sepsis, showed *Staphylococcus pyogenes* only.

In the first two of these patients, the initial iridocyclitis was of considerable severity, but the subsequent history was consistent with a steady improvement after the removal of the infections in the teeth and sinuses, the poor final result being due to the damage inflicted by the initial attack. The third patient, however, retains an active cyclitis in spite of removal of the infections, which are presumably, therefore, coincidental.

In view of the relatively better prognosis in patients who were adequately treated, the response to antibiotic treatment in patients with *Streptococcus haemolyticus* infection would be of considerable interest. In the three such patients who had had a recurrence of uveitis after cessation of ocular treatment, the effect of elimination of the streptococcal infection in preventing recurrences could only be assessed over a long period, and cannot be usefully discussed further at present. Of the three patients still under treatment at the time of the follow-up survey, one had a shrunken eye following operations for secondary glaucoma and a swollen lens, and the uveitis in one patient subsided 3 months later so that mydriasis could be discontinued; the third (Case 7) was the only patient in whom antibiotic treatment appeared to be worthwhile.

Case 7, a female aged 64 years, had bilateral anterior uveitis in which pan-uveitis could not be excluded; she was highly myopic with central degenerative changes. The only significant finding on investigation was *Streptococcus haemolyticus* in the throat cultures. She developed secondary glaucoma in one eye, but this was controlled with Diamox. In September, 1956 *Streptococcus haemolyticus* was still present in the throat swab but was eliminated by systemic penicillin therapy; there was subsequently a diminution in the number of keratic precipitates, which were becoming pigmented, and slit-lamp examination showed only a very faint aqueous flare. Diamox was discontinued in November, 1956, and there had been no rise in ocular tension one month later.

It is obviously not possible to draw firm conclusions from these patients, but the findings are at any rate not inconsistent with the supposition that in many patients granulomatous anterior uveitis and pan-uveitis are caused by the associated infection; elimination of such infections would appear to be well worth further trial in these types of uveitis.

III. SYSTEMIC DISEASES

BY

A. STANWORTH

Those patients in whom uveitis was considered to be associated with local or general disease have already been described. In a number of other patients, less definite associations were found.

Venereal Diseases

In two patients, syphilis was suspected to be a possible cause of uveitis.

Case 8, a male aged 68 years, with non-granulomatous anterior uveitis, had a positive Wassermann reaction and Kahn test, but he also had untreated diabetes mellitus and pneumococcal throat infection, and the syphilis may have been coincidental.

Case 9, a female aged 32 years, with recurrent granulomatous anterior uveitis, had congenital syphilis; she had been found elsewhere in 1948 to have a positive Kahn test but a negative Wassermann reaction, and had been treated with penicillin injections but had defaulted; in 1954 the Kahn test was positive but unstable, and again she defaulted after four injections; she had parodontal infection, and evidence of old tuberculous apical lung infection.

A history of treated syphilis leading to a negative Wassermann reaction was given by three patients, one with typical ankylosing spondylitis, one with Reiter's disease with radiographic evidence of spinal arthritis, and one with Reiter's disease without radiographic spinal changes.

The gonococcal complement-fixation test was performed on serum from 205 patients, and was found to be positive or strongly positive in seven. Two of these had uveitis ascribed to syphilis, and two had spondylitis. The remaining three patients all had anterior uveitis.

Case 10, a male aged 52 years, with granulomatous anterior uveitis, had a strongly positive gonococcal complement-fixation test, *Streptococcus haemolyticus* in the throat cultures, and radiological evidence of active chest tuberculosis; he refused further investigation and treatment.

Case 11, a female aged 70 years, with bilateral granulomatous anterior uveitis, had a strongly positive gonococcal complement-fixation test, which, on repetition, was only doubtfully positive; the venereologist thought the condition was unlikely to be gonococcal.

Case 12, a female aged 42 years, with non-granulomatous anterior uveitis, was also seen by the venereologist, who considered that she could have had chronic gonococcal infection, but that there was no definite evidence.

In 25 patients the gonococcal complement-fixation test gave a doubtful result; it was repeated in seventeen patients, and was then found to be negative in eleven, still doubtful in five, and positive in one. It was considered by the venereologist that the positive reaction was unlikely to be due to gonococcal infection in the last patient, who has already been described (Case 1). In four patients (Cases 8, 9, 10, and 12), therefore, the uveitis may have been of venereal origin.

Diabetes

Seven patients had diabetes; two had had treatment, one by diet only, but neither was fully controlled. One patient with syphilis (Case 8) has already been described; one **(Case 13),** who had anterior uveitis of doubtful type, also suffered from albuminuria and uraemia from which he died, but no *post-mortem* examination was carried out; one had uveitis associated with superficial punctate keratitis and *Streptococcus haemolyticus* infection in the throat. The remaining four patients had anterior uveitis, one granulomatous and three of doubtful type; all cultures were negative in two, nasal sinus infection was absent in three, and parodontal infection was absent in three. There was therefore no evidence that uveitis had been produced in these patients by any greater liability to septic infections.

Three of the patients were more than 70 years of age, two were between 61 and 70 years (Cases 8 and 13), and two were between 41 and 50 years. The diabetes was therefore likely to be largely of the senile type, and may well have been coincidental in the majority of patients.

Tuberculosis and Sarcoidosis

Radiography of the chest was performed in 202 patients, and the Mantoux reaction to 0·1 mg. and to 0·01 mg. of human old tuberculin in 211 patients, the diameter of the reaction of oedema being recorded as + (less than 10 mm.), + + (10–19 mm.), or + + + (20 mm. or more).

Definite sarcoidosis was diagnosed in two females with granulomatous anterior uveitis; the Mantoux reaction was negative in one, and + to 0·1 mg. in the other, in whom it had been reported as negative 2 months previously. In two others the clinical picture raised the possibility of sarcoidosis.

Case 14, a female aged 26 years, with anterior uveitis of doubtful type and secondary glaucoma resembling the Posner-Schlossman syndrome, had radiographic enlargement of the hilar and right paratracheal lymph glands which could have been due to sarcoid or one of the reticuloses; the Mantoux reaction was negative; radiography of the hands and feet was negative, and the serum proteins were normal.

Case 15, a female aged 66 years, with granulomatous anterior uveitis, had an unexplained loss of weight of up to 3 stones at the time she had uveitis; a radiograph of the chest was reported to show "fine modulation in the lung fields; this is not quite definite but raises the possibility of sarcoidosis". A further radiograph one month later showed no abnormality, and the Mantoux reaction was positive (+++ to 0·01 mg.), so that a diagnosis of sarcoidosis was unlikely.

Possibly active tuberculous lesions were found in three patients. One (Case 10) had a strongly positive gonococcal complement-fixation test; the others are described below.

Case 16, a female aged 41 years, with bilateral anterior uveitis of doubtful type with secondary glaucoma, had radiographic evidence of old tuberculous chest lesions in which activity could not be excluded, but the patient defaulted.

Case 17, a male aged 70 years, with granulomatous anterior uveitis, suffered from lupus vulgaris and psoriasis. Chest radiographs showed emphysema only; he had a positive differential agglutination test for rheumatoid arthritis, but did not attend for further examination.

No effort was made to record all traces of possible previous tuberculous chest disease, but obvious radiographic evidence of old apical lesions was recorded in fourteen patients, calcified hilar lesions in five patients, and old pleural reactions at the lung bases in five patients. There was a slight tendency, not statistically significant, for the apical and hilar lesions to occur more commonly in anterior uveitis of granulomatous and doubtful types, and this was more marked in the basal pleural lesions, so that when all the patients with old lung lesions were considered, the increased incidence in these types of uveitis (twelve in 57 radiographs) was significant ($\chi^2 = 5{\cdot}1$; $P = 0{\cdot}03$) when compared with the remainder of the series (twelve in 145 radiographs). There was, however, no certainty that all these lesions, especially the basal ones, were in fact tuberculous.

The distribution of the Mantoux reactions, excluding the three patients with definite or probable sarcoidosis, is shown in Table XIV (overleaf); there was an increased incidence of negative reactions in patients with granulomatous anterior uveitis of no known association, but this was not statistically significant; in none of these patients was the clinical picture suggestive of sarcoidosis.

There was a tendency, again not significant, for an increased incidence of positive Mantoux reactions to 0·01 mg. in patients with non-granulomatous anterior uveitis; this was due almost entirely to the high proportion of such reactions in the age group 21–40 years (sixteen out of the seventeen patients), which was significantly higher ($\chi^2 = 4{\cdot}6$; $P = 0{\cdot}04$) than that in the remainder of the age group (36 out of 57); it was still significantly high if the relatively

TABLE XIV
MANTOUX REACTION

Association with Local or General Disease*			Kerato-uveitis	Anterior Uveitis			Posterior Uveitis	Pan-uveitis	Total
				Granulo-matous	Non-granulo-matous	Doubtful Type			
Known Association	Non-rheumatic	No. Tested	11	2	2	—	—	—	15
		Negative	3	1	—	—	—	—	4
		+ to 0·1 mg.	1	—	—	—	—	—	1
		+ to 0·01 mg.	7	1	2	—	—	—	10
	Rheumatic	No. Tested	2	1	21	8	1	—	33
		Negative	—	—	2	—	1	—	3
		+ to 0·1 mg.	—	—	5	3	—	—	8
		+ to 0·01 mg.	2	1	14	5	—	—	22
No Known Association		No. Tested	16	42	56	15	28	3	160
		Negative	3	10	6	2	5	1	27
		+ to 0·1 mg.	3	8	8	3	6	2	30
		+ to 0·01 mg.	10	24	42	10	17	—	103

* Three patients with sarcoidosis are excluded

increased proportion of negative reactions in granulomatous anterior uveitis was allowed for by omitting this entire group ($\chi^2 = 4{\cdot}1$; $P < 0{\cdot}05$). The distribution of the Mantoux reaction is shown in the Figure; the patients with rheumatic disease show an increased incidence of positive reactions, as have been described in ankylosing spondylitis by Robinson (1940), but this increase was not so marked as in non-granulomatous anterior uveitis of no known association. In the series as a whole, there was a general tendency

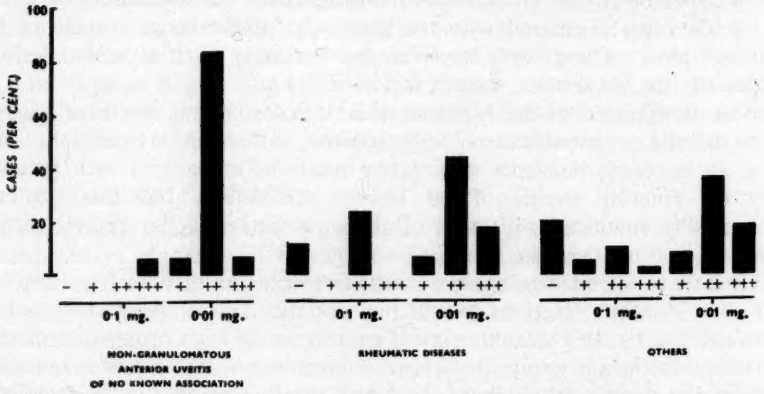

FIGURE.—Mantoux reaction in patients aged 21 to 40 years (excluding one patient with probable sarcoidosis).

to a higher proportion of positive reactions in males, but the high incidence of positive Mantoux reactions to 0·01 mg. in non-granulomatous anterior uveitis of no known association in the age group 21–40 years occurred in both sexes (in twelve of thirteen males, and in all of the four females).

Periarteritis Nodosa

This disease was suspected in two patients described elsewhere (Stanworth and Sharp, 1956), one with posterior uveitis and one with granulomatous anterior uveitis; the latter had no upper respiratory tract infection and appeared to be edentulous, but was not seen by the dental surgeon.

Erythema Circinata

A female aged 48 years with non-granulomatous anterior uveitis had had recurrent erythema circinata since the age of 18 years; she had throat infection with *Streptococcus haemolyticus*; the Mantoux reaction was negative.

Toxoplasmosis

The dye test for toxoplasmosis, using the modification described by Beverley and Beattie (1952), was carried out on seventeen patients in this series. Nine had posterior uveitis, which was generalized in four, focal in three, and associated with retinal perivasculitis in two; one of the latter, described by Stanworth and Sharp (1956), had Reiter's disease. The small number of tests was due to the fact that experience of the dye test in Manchester since the end of 1952 had revealed very few patients with a positive test; following the report by Woods, Jacobs, Wood, and Cook (1954) that 25 per cent. of cases of granulomatous uveitis appeared to be due to toxoplasmosis, routine testing of patients was started in this series in April, 1954, but was largely confined, in order to conserve both time and material, to those patients who appeared most likely to have positive reactions, *i.e.* those with granulomatous posterior uveitis or pan-uveitis; the ten patients with posterior or pan-uveitis who had the dye test carried out comprise two-thirds of such patients seen since that date.

The test was positive to a titre of at least 1/16 in a girl aged 14 years with focal choroidoretinitis, and to a titre of 1/4 in a male aged 58 years with recurrent generalized posterior uveitis since 1915, who had also suffered from recurrent amoebiasis and from strongyloides infection. In the remaining eight patients, the dye test was negative, as it was in five patients with non-granulomatous anterior uveitis (two of whom had evidence of ankylosing spondylitis, one with radiographic spinal changes), in one with granulomatous anterior uveitis, and in two with kerato-uveitis (one of whom had herpes zoster ophthalmicus).

These results differ greatly from those reported by Smith and Ashton (1955) and by Perkins, Smith, and Schofield (1956); in both these series, the tests had been done by the same method but in a different laboratory (Department of Bacteriology, University of Sheffield); in view of the reported

erratic value of the results of the dye test on individual sera (Lelong and Desmonts, 1952; Goldman, 1956), the tests were repeated in Sheffield on stored sera from sixteen of the eighteen patients (in two patients (one of whom had the titre of 1 in 16) the sera had deteriorated and were useless for further testing). The results were quite different from those originally obtained: in six patients with generalized or focal choroidoretinitis, the test was positive at titres of 1 in 58, 1 in 40 (previously 1 in 4), 1 in 20, 1 in 16, 1 in 13, and 1 in 5; in perivasculitis, it was positive at titres of 1 in 20 (the patient with Reiter's disease) and 1 in 19; in non-granulomatous anterior uveitis, it was positive in two patients with titres of 1 in 14 (ankylosing spondylitis without radiographic changes) and 1 in 6 (ankylosing spondylitis with radiographic spinal changes), and negative in two; in the patient with granulomatous anterior uveitis it was negative; in both patients with kerato-uveitis it was positive, with titres of 1 in 100 (the patient with herpes zoster ophthalmicus) and 1 in 18. The test was negative in a patient with pan-uveitis who was not tested in Manchester. The complement-fixation test was only possible in five patients (dye test titres 1 in 58, 1 in 20, 1 in 13, 1 in 6 and <1 in 4), and was negative in all five.

Leptospirosis and Brucellosis

No suggestion of these diseases was obtained from the history of any patients; the leptospira agglutination test was negative in eighteen patients.

Allergy

A history of allergy was obtained in nine patients: four had asthma (one also with allergic dermatitis), four had hay fever, and one gave a history of allergy to penicillin. One patient with severe chronic kerato-uveitis had skin tests for allergy and was found to be markedly sensitive to inhalants, but desensitization and antihistamine therapy did not appear to affect the course of the disease. One patient had atypical spondylitis, one had posterior uveitis, and five had anterior uveitis (non-granulomatous in one, of doubtful type in one, and granulomatous in three, two of the latter being associated with infection). It appears, then, that the overall incidence is probably not appreciably different from that in the general population, and an allergic history was not associated with any one type of uveitis.

Virus Diseases

In addition to the sixteen patients with uveitis of definite virus origin (herpes zoster ophthalmicus and dendritic ulceration), uveitis was associated with superficial punctate keratitis in six patients, one of whom had Reiter's disease with radiographic evidence of spinal changes.

Evidence of possible preceding abacterial conjunctivitis or keratitis, such as Bennett (1955) considers to be due to virus infection, was obtained in twelve patients with anterior uveitis, one of whom had radiographic evidence of ankylosing spondylitis; of the remainder, the uveitis was granulomatous

in two patients, non-granulomatous in five, and of doubtful type in four. Four patients gave a history of mild ocular trauma, such as Bennett (1955) considers may precipitate a virus infection. One had ankylosing spondylitis, two others had non-granulomatous anterior uveitis, and one had granulomatous anterior uveitis associated with parodontal sepsis. On this basis, the maximum incidence of diagnosable virus infection in anterior uveitis was 9 per cent. (sixteen in 170 patients); if kerato-uveitis is included, the incidence rises to 19 per cent. in anterior uveitis (38 in 205 patients) or to 16 per cent. in the whole series. This is much lower than the figure of 38 per cent. given by Bennett (1955), which obviously includes many patients in whom a virus origin of uveitis is far from proved.

Serum Proteins and Erythrocyte Sedimentation Rate

Serum proteins were estimated in 204 patients, and a globulin content of more than 3·5 mg. per cent. was noted in 41 patients. One of the systemic diseases already discussed, including the rheumatic diseases, could reasonably be held responsible in 25 of these 41 patients; one was pregnant; one had uveitis due to rupture of the lens capsule; repetition of the test in four patients gave a normal result. The highest serum globulin content in the remaining ten patients was 4 mg. per cent., and none of them had granulomatous anterior uveitis.

The erythrocyte sedimentation rate was measured in 207 patients, and was found to be raised in 67 patients. One of the diseases already discussed could reasonably be held responsible in 48 patients; there was no evidence of serious systemic disease in the remaining patients, and there was no obvious tendency for them to have any particular variety of uveitis.

Uveitis possibly due to Systemic Diseases

In addition to the patients already described with a known local or general disease, eleven may also have had a systemic disease, other than spondylitis, related to their uveitis, namely three with venereal disease (Cases 8, 9, and 12), one with venereal disease and active tuberculosis (Case 10), one with sarcoidosis (Case 14), two with possibly active tuberculous lesions (Cases 16 and 17), one with diabetes and terminal uraemia (Case 13), two with polyarteritis nodosa, and one with erythema circinata. The possible importance of toxoplasmosis will be discussed later. Ten of the eleven patients had anterior uveitis (which was granulomatous in four, non-granulomatous in three, and of doubtful type in three), and one had posterior uveitis. In addition, six patients with granulomatous anterior uveitis had radiological evidence of inactive chest lesions that could have been tuberculous; these were apical in two, hilar in two, and basal in two.

IV. DISCUSSION

BY

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Rheumatic Diseases

Ankylosing spondylitis and atypical forms of spondylitis are the largest single group of systemic diseases with which uveitis has been found to be associated in this survey (Stanworth and Sharp, 1956; Stanworth, 1956); these forms of spondylitis are relatively rare, and an incidence of 37 radiologically proved cases in 237 patients is undoubtedly of great significance. It is therefore surprising that so little interest has been taken in this association; Woods (1956b), for example, in an exhaustive manual designed for teaching purposes, omits all mention of the rheumatic diseases, and Dekking (1954) considers the association to be no more than an interesting coincidence. Both these authors believe that streptococcal infection is aetiologically related to non-granulomatous uveitis; if this be the case, there are three possible assumptions regarding the rheumatic disease:

(*i*) Non-granulomatous uveitis and rheumatic disease are associated by chance. This is unlikely in view of the closeness of the association, for at least two-fifths and possibly one-half of the males with non-granulomatous anterior uveitis had spondylitis (Stanworth and Sharp, 1956).

(*ii*) Non-granulomatous uveitis and rheumatic disease are both responses to streptococcal infection. This is affirmed by Woods (1953), largely on the evidence of skin sensitivity tests with streptococcal vaccines in non-granulomatous uveitis and of streptococcal agglutination and precipitin titres in rheumatoid arthritis. In common with other American authors (Bauer, 1939; Boland and Present, 1945; Hench, Slocumb, and Polley, 1947), he presumably considers ankylosing spondylitis to be a variant of rheumatoid arthritis involving the spine; in Great Britain, however, it is considered to be a separate disease, and the significant association with non-granulomatous anterior uveitis, in contrast to the lack of marked association between classical rheumatoid arthritis and any form of uveitis, is in accordance with this view. According to Buckley (1955), ankylosing spondylitis is probably of infective origin, the focus probably being always pelvic but frequently not venereal. Buckley considered infection from the intestine to be the source in many cases; West (1949) considered that the disease might be related to a local metabolic defect in articular structures subjected to continuous stress, with heredity as a major aetiological factor. Reiter's disease, which in its later stages may give a picture indistinguishable from ankylosing spondylitis (Ford, 1953), may also be due to pelvic infection, either urethral or intestinal, possibly by a virus (Harkness, 1950). In any case, there is a considerable body of opinion that there is no acceptable evidence that infection is directly or indirectly the cause of rheumatoid arthritis (Duthie and Davidson, 1955); and in ankylosing spondylitis the streptococcal agglutination and precipitin titres are normal (Levinthal, 1938), as is the antifibrinolysin titre (Perry, 1940).

(*iii*) These rheumatic diseases, though not in themselves related to streptococcal

infection, may predispose the patient to uveitis due to such infection. This would lead one to expect a high incidence of streptococcal infection in non-granulomatous uveitis, but that has not been found to be the case in this survey in patients either with or without rheumatic disease.

There remains the possibility that a connexion exists between non-granulomatous uveitis and a factor common to the various forms of spondylitis, perhaps related to the spinal involvement. Such a factor might be present only in patients with rheumatic disease, or in many other patients with non-granulomatous anterior uveitis; in favour of the former is the fact that spinal arthritis affects mainly males, whereas the non-rheumatic patients with non-granulomatous anterior uveitis showed no particular sex distribution. This suggests that there may be two factors in the aetiology of this type of uveitis, one affecting mainly males and associated with spinal involvement, and a second unrelated to rheumatic disease and not sex-linked. Whether or not this supposition is true, it remains of importance to pay considerable attention to the connexion between uveitis and rheumatic disease.

Rheumatic Fever.—The failure to find any relationship between rheumatic fever and uveitis, in spite of the association between granulomatous anterior uveitis and *Streptococcus haemolyticus* infection, may be due to the fact that rheumatic fever is usually associated with Group-A *Streptococcus haemolyticus* infection (Horder and Bywaters, 1955), whereas the association found in the present survey was mainly with streptococci not in Group A.

Tuberculosis

The proportion of uveitis ascribed to tuberculosis has varied widely with different observers, but there has been a tendency to consider it of less and less importance in the last 20 years; thus Guyton and Woods (1941) found that 79 per cent. of granulomatous uveitis was due to tuberculosis, Woods and Guyton (1944) 52 per cent., and Woods, Jacobs, Wood, and Cook (1954) only 23 per cent. The criteria for the diagnosis of ocular tuberculosis (Woods 1956b) are still largely dependent on the exclusion of other causes; moreover, of the more positive indications of tuberculosis, focal ocular reactions to tuberculin could be non-specific, and an association of uveitis with deep scleritis or sclero-keratitis may be due to other causes—for example, to nodular rheumatoid arthritis. It appears therefore, that the role of tuberculosis is still very much in doubt; in the present series, it was impossible to be certain that any patient had tuberculous uveitis, and only eight patients with granulomatous anterior uveitis or pan-uveitis had sufficient radiographic evidence of either active or old chest lesions to justify comment by the radiologist.

In patients without proved rheumatic disease or any known cause for their uveitis, the association between non-granulomatous anterior uveitis and a markedly positive Mantoux reaction is of considerable interest, particularly in view of the reported sensitivity of this type of patient to skin tests with

streptococcal vaccines (Woods, 1950, 1953, 1956a). This suggests that both these skin reactions may be due to a non-specific tendency of these patients to show markedly positive skin tests to a variety of agents, and is reminiscent of the similar tendency to a high level of reaction to tuberculin among patients with ankylosing spondylitis (Robinson, 1940).

Toxoplasmosis

The evidence that toxoplasmosis is a cause of uveitis is mainly statistical. Toxoplasma antibodies are found more frequently in persons who have uveitis than in those who have not. Thus Perkins and Beverley (1957) found toxoplasma dye test antibodies present to a titre of 1 in 4 or more in over 60 per cent. of patients with uveitis but in only 30 per cent. of normal people. The difference was particularly marked in the younger age group. Under the age of 20 years toxoplasma antibodies were found in 60 per cent. of patients with uveitis and in less than 10 per cent. of others. The statistical evidence is supported by the isolation of toxoplasma from the retina and choroid (Jacobs, Fair, and Bickerton, 1954), and by its demonstration in histological sections (Wilder, 1952a, b; Duke-Elder, Ashton, and Brihaye-van Geertruyden, 1953).

While serological evidence has been of great value in establishing statistically that toxoplasmosis is a cause of uveitis, it is of much less value in making a diagnosis of toxoplasmic uveitis in an individual patient. A negative result, at any rate from tests carried out in Sheffield, can be taken to exclude it, but a positive result, even to a high titre, does not prove it. All that can be said is that in a child the presence of antibodies, particularly if they be of high titre, makes it very likely that the uveitis is due to toxoplasmosis. In an adult a positive test, especially in high titre, obviously increases the chance of the condition being toxoplasmic, but the whole clinical picture has to be taken into account.

Jacobs, Naquin, Hoover, and Woods (1956) indicate that a dye test of 1 in 64 or more may be taken as significant; but Beattie (1957) found that 12 per cent. of normal adults in rural areas and 5 per cent. in urban areas in Great Britain had antibodies to this titre. Smith and Ashton (1955) ascribed equal significance to a positive dye test at any level; in support of this, it may be mentioned that Jacobs, Cook, and Wilder (1954) found titres of less than 1 in 64 in cases of ocular toxoplasmosis. Perkins, Smith, and Schofield (1956) think that toxoplasmosis is probably the cause of the uveitis in 25 per cent. of patients with any level of toxoplasma antibody. This applies most strongly to patients with posterior uveitis, in whom positive results in low titres occurred much more commonly than in the general population, and it appeared unlikely that cases of generalized uveitis were due to toxoplasmosis.

In the present series, the serum of only one patient had antibodies to a titre of 1 in 64 and in her case the kerato-uveitis was undoubtedly due to

herpes zoster ophthalmicus. Three patients with focal choroidoretinitis approached this level: one with a titre of at least 1 in 16 (tested in Manchester), and two with titres of 1 in 58 and 1 in 40 (tested in Sheffield).

The variations in titre obtained in different tests on the same sera, together with the occurrence of positive tests in herpes zoster ophthalmicus and ankylosing spondylitis in the present series and in that of Davenport (1955), indicate that, in any individual patient, the interpretation of low titres can be difficult or impossible.

ALLERGY

The failure to find any obvious association between uveitis and hay fever or asthma does not necessarily mean that other forms of allergy may not be of importance; there may well be a fundamental distinction between the immediate allergic response, such as hay fever and urticaria, and the delayed responses, such as bacterial allergy (Pickering, 1952).

FOCAL INFECTION

The strong association of parodontal, nasal sinus, and *Streptococcus haemolyticus* infections with granulomatous anterior uveitis was mainly with the very chronic type, and with those patients in whom pan-uveitis could not be excluded. This is of interest since, as we have already noted, Perkins, Smith, and Schofield (1956) found that it was unlikely that cases of generalized uveitis are due to toxoplasmosis, and the absence of tests for toxoplasmosis in these patients is therefore probably of little significance.

If it is considered that focal infection occurs only by chance in those patients whose uveitis was possibly due to systemic disease (including those with radiological evidence of old chest lesions), or who had heterochromic cyclitis or the Vogt-Koyanagi syndrome, there still remain, in patients fully investigated, sixteen patients with infection out of 22 with granulomatous anterior uveitis of no known association, compared with 51 out of 122 patients in the remnants of the series; this difference is still significant ($\chi^2 = 6{\cdot}0$; $P < 0{\cdot}02$); it appears likely, therefore, that the association with infection is of more importance than the rather nebulous connexion with systemic diseases in many of these patients.

The finding of a strong association between focal infection and granulomatous anterior uveitis is contrary to the experience of Woods (1953, 1956a), who found foci of infection in only 30 per cent. of granulomatous uveitis compared to 54 per cent. of non-granulomatous uveitis; there are, however, several factors which may explain the difference.

In the first place, the criteria of significant focal infection in the present series (namely parodontal, nasal sinus, and *Streptococcus haemolyticus* infection) have been evolved as a result of analysis of the series itself, and may well be very different from those employed by Woods.

Secondly, the classification of uveitis is different, for Woods takes no

account, in his subdivision into granulomatous and non-granulomatous, of the subdivision into anterior and posterior, of the presence or absence of rheumatic disease or other known associations, or of age or sex.

Thirdly, it is probable that the patients reviewed by Woods did not form a random series, since they were "referred to the Wilmer Institute for study, to determine, if possible, the cause of the uveitis". They may therefore have included a higher proportion of patients with a poor prognosis or recurrent attacks. For example, Woods states that, in non-granulomatous uveitis, "recurrences, spaced at intervals from a few weeks to many months, are the rule rather than the exception" (Woods, 1953). In contrast to this, only seven of the 26 patients with rheumatic disease in the present series, and twelve of the sixty without such disease, could be said, on the basis of their previous history and subsequent progress during a follow-up period averaging 33 months, to have recurrences at intervals measured in months, rather than in years; and in almost half the patients with rheumatic disease and two-thirds of those without such disease, the attack of non-granulomatous uveitis for which they originally attended was a completely isolated one. This difference in the frequency of recurrent attacks does not, however, fully explain the disparity in the findings, since there was no apparent difference, in the present series, in the incidence of focal infection between those patients with and those without frequent recurrences.

Woods (1956b) takes the view that there is no evidence that foci of infection in the body can produce an effect on the uvea except by a hypersensitivity phenomenon. He has himself pointed out, however, "that bacteria do constantly enter the blood stream in small numbers in normal persons. For example, colon bacilli can often be cultivated from the portal vein; pyelitis develops with amazing regularity if there is an obstruction to the ureter, and the source of infection can be conclusively traced to intermittent bacteraemia, the kidney being infected only because predisposed by the local condition" (Guyton and Woods, 1941). These facts indicate that bacterial metastasis, with or without superadded allergic reactions, cannot be ruled out. Absence of positive blood cultures in uveitis is not conclusive evidence against this, since negative cultures are common, even in known bacteraemia such as subacute bacterial endocarditis.

Woods (1956b) also considers that uveitis related to focal sepsis is always of a non-granulomatous type; a granulomatous type of reaction can, however, occur as a result of infection with pyogenic organisms, as may be seen in vegetating pyoderma and the granulomatous lesions of parodontal sepsis (Montgomery, 1953).

If bacterial metastasis be an aetiological factor, the failure to find an association between granulomatous anterior uveitis and periapical sepsis suggests that it is the presence of a relatively large area of infection which is of importance, rather than the more compact infection found in periapical disease, even though the latter may contain pus under pressure. The failure

to find any localization of parodontal infection to the upper jaw on the same side as the uveitis also supports a connexion *via* the blood stream rather than *via* the nasal sinuses or the lymphatic glands. The duration of the infection may also be of importance; this would explain why the associations with nasal sinus and *Streptococcus haemolyticus* infections were more marked in elderly people, whereas parodontal sepsis exerted its main influence before the age at which the teeth are likely to be lost.

It is not surprising that, in surveys of infection in uveitis as a whole (Guyton and Woods, *1941; Bennett, 1955*), no obviously increased incidence of focal sepsis was found, for it is only in granulomatous anterior uveitis and pan-uveitis that the association has been found in this survey, and these comprised only 23 per cent. of the whole. Moreover, it is possible that upper respiratory tract infections may, like chronic bronchitis, be more common in the north-west region of England, due perhaps to the high humidity accompanied by smoke (Goodman, Lane, and Rampling, 1953), so that infection as a cause of granulomatous anterior uveitis may be of less significance outside this area.

The failure to find an association between streptococcus infection and non-granulomatous anterior uveitis does not, in itself, necessarily override the evidence obtained from skin tests and from studies of the anti-streptolysin titres; nevertheless, as we have seen, these studies may be misleading (Otten and Westendorp Boerma, 1954); moreover Woods (1953a) considered that *Streptococcus haemolyticus* belonging to Lancefield Group-A is of considerable importance, in which case it is surprising that there is no obvious connexion between uveitis and rheumatic fever, a disease which is undoubtedly associated with raised anti-streptolysin titres following infections with this organism (Gibson, 1955; Horder and Bywaters, 1955).

Endogenous Uveitis

This investigation has not thrown any new light on the aetiology of kerato-uveitis, except to confirm that occasionally uveitis may be associated with transient superficial punctate keratitis, possibly of virus origin, and sometimes with Reiter's disease. If kerato-uveitis be excluded, together with those patients suffering from herpes zoster ophthalmicus, sympathetic ophthalmia, and rupture of the lens capsule, 197 patients with "endogenous" uveitis remain. Associations with general disease are shown in Table XV (overleaf), a patient with more than one association being included only under that disease which appears first in the Table. Had all the patients been fully investigated, the number with no known association could be expected to be diminished to some extent, but almost half the total number would still remain with no known association.

Of these, almost half had non-granulomatous anterior uveitis; it is suggested that further attention should be paid to the relationship of this type

TABLE XV
ENDOGENOUS UVEITIS*

Association with General Disease			Anterior Uveitis			Posterior Uveitis	Pan-uveitis	Total
			Granulomatous	Non-Granulomatous	Doubtful Type			
Known Association	Significant	Syphilis	—	2	—	—	—	2
		Sarcoidosis	2	—	—	—	—	2
		Rheumatic Disease	1	26	8	1	—	36
		Focal Infection	26	—	—	—	2	28
		Total	29	28	8	1	2	68
	Possibly Significant	Toxoplasmosis ...	—	—	—	3	—	3
		Syphilis	—	1	—	—	—	1
		Sarcoidosis	—	—	1	—	—	1
		Rheumatic Disease ...	1	11	2	2	—	16
		Focal Infection ...	3	—	—	—	—	3
		Gonorrhoea ...	—	1	—	—	—	1
		Tuberculosis ...	3	—	1	—	—	4
		Diabetes and Uraemia	—	—	1	—	—	1
		Total	7	13	5	5	—	30
No Known Association			13	47	15	23	1	99
TOTAL			49	88	28	29	3	197

* Patients with kerato-uveitis, herpes zoster ophthalmicus, sympathetic ophthalmitis, and ruptured lens capsule excluded

of uveitis to rheumatic diseases and to the tendency to react excessively to a variety of agents (*e.g.* tuberculin, streptococcal vaccines).

In granulomatous anterior uveitis and pan-uveitis, further studies are obviously needed to confirm the suggested causal importance of focal infection, and to study the organisms involved in the parodontal and nasal sinus infections.

In posterior uveitis, toxoplasmosis may account for a number of the patients not so far definitely diagnosed, but there may well be regional variations in the incidence of the disease, as there are in such causes of uveitis as brucellosis and leptospirosis.

The correlations established between non-granulomatous anterior uveitis and rheumatic disease on the one hand, and between granulomatous anterior uveitis, pan-uveitis, and focal infection on the other hand, tend to suggest that it is of value to distinguish between the granulomatous and non-granulomatous types of uveitis; nevertheless, the conclusions reached in this survey would be substantially unaltered if the uveitis had been classified simply into acute and chronic, and it is undoubtedly true that the distinction between granulomatous and non-granulomatous types is not an absolute one (Ashton, 1954).

Summary

(1) 237 consecutive patients with uveitis were investigated.

(2) Granulomatous anterior uveitis was found to be associated with parodontal and nasal sinus infections, and with the presence of *Streptococcus haemolyticus* in nasal and throat cultures. The association was more marked in those patients in whom the uveitis was obviously of a chronic type, and in whom pan-uveitis could not be excluded. The response to treatment was not inconsistent with a causal connexion.

(3) Positive cultures for pneumococci were associated with anterior uveitis in younger patients; a particular association with the granulomatous type was less certain. No definite evidence of other significant infections was found.

(4) The pathogen selective test was of no value in predicting which organisms were related to uveitis.

(5) Non-granulomatous anterior uveitis was associated with strongly positive Mantoux reactions; this may be evidence of a general non-specific tendency to react to a variety of agents. There may be two factors in the aetiology of this type of uveitis, one affecting mainly males and associated with various forms of spondylitis, and a second unrelated to rheumatic disease and not sex-linked.

(6) The importance ascribed to toxoplasmosis depends on the criteria employed; venereal diseases, tuberculosis, and sarcoidosis accounted for only a small number of cases; diabetes was largely coincidental.

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CORNEAL RADIUS IN PRIMARY ACUTE GLAUCOMA*

BY

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EXCEPT in hydrophthalmos very little is known about the size and shape of the cornea in glaucoma. About 100 years ago von Helmholtz (1855) and von Graefe (1857) supposed that the corneal radius increased when the intraocular pressure was rising. They thought that the shallow anterior chamber found in acute congestive glaucoma could be explained in this way. However, when measurements were made, no increase or only insignificant increases of the radius could be demonstrated. The shallow anterior chamber is probably the result of genetic factors creating a structure of the eye predisposing to acute glaucoma but not produced by the acute attacks themselves (Rosengren, 1930, 1931; Törnquist, 1953, 1956a, b).

No systematic investigations concerning the radius of curvature of the cornea in glaucomatous eyes as compared to normal eyes have been made. The transverse corneal diameter was measured by Smith (1890), who found that it was, on an average, about 0·5 mm. smaller in glaucomatous eyes than in normal eyes. The small cornea was thought to be combined with a small eyeball, and a disproportion in size between the corneo-scleral capsule and the lens was considered to be a predisposing factor in glaucoma.

In the present paper a comparison is presented between the radius of curvature of the cornea in a series of cases of acute glaucoma and that in a series of normal eyes. The purpose is to elucidate the problems of the specific structure of the eye in this disease.

Method

The radius of curvature of the cornea was measured along the two principal meridians with a Javal-Schiötz ophthalmometer (Haag-Streit). The readings were made to within 0·05 mm. In astigmatism the average of the two radii was recorded.

Material

The chamber depth was measured in a series of 146 eyes from 95 patients with primary acute glaucoma (Törnquist, 1956b), and in these eyes the corneal radius was also recorded. The corneal radius was also measured in a series of 398 normal eyes of persons aged 20–65 years. The chamber depths of these eyes had been reported previously (Törnquist, 1953). This series comprised a representative selection of subjects with regard to distribution of age, sex, and refractive errors.

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Results

The corneal radius in the series of normal eyes and eyes with acute glaucoma is shown in the Figure and Table I. There seems to be no significant deviation from the normal distribution in either series. The mean of the normal subjects is 7·78 ± 0·015 mm. (standard deviation 0·29 mm.). These values agree with those found in earlier investigations (Hess, 1903; Stenström, 1946). In the glaucomatous eyes the mean is 7·53 ± 0·023 mm. (standard deviation 0·27 mm.). The difference between the two means is 0·25 ± 0·027 mm. and thus statistically significant.

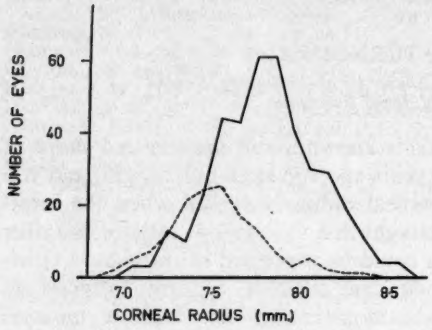

FIGURE.—Corneal radius in a series of 398 normal eyes (whole line) and 146 eyes with acute glaucoma (dotted line).

Acute glaucoma is more frequently found in elderly women than other individuals (Törnquist, 1956a). The present series also contains a majority of females (71:24), and thus, the sex distribution is not the same as in the normal series. According to Stenström (1946), the corneal radius seems to be smaller in females than in males and it is possible that this explains to some extent the dissimilarity between the glaucomatous and the normal series. However, when the glaucoma series is compared with the elderly women of the normal series (98 females aged 50–65 years) the difference is still significant (Table II).

TABLE I
CORNEAL RADIUS IN EYES WITH ACUTE GLAUCOMA AND IN NORMAL EYES

Eyes	Number	Average Corneal Radius (mm.)
Glaucomatous	146	7·53 ± 0·023
Normal	398	7·78 ± 0·015
Difference		0·25 ± 0·027

TABLE II
CORNEAL RADIUS IN EYES WITH ACUTE GLAUCOMA AND IN NORMAL EYES OF WOMEN AGED 50–65 YR.

Eyes	Number	Average Corneal Radius (mm.)
Glaucomatous	146	7·53 ± 0·023
Normal	98	7·82 ± 0·033
Difference		0·29 ± 0·040

There seems to be no correlation between the corneal radius and the chamber depth in normal eyes (Stenström, 1946). Table III shows a comparison between 57 normal eyes with a chamber depth of the same magnitude as the majority of the glaucomatous eyes (1·5–2·1 mm.) and 76 eyes with acute glaucoma and a chamber depth between the same limits. The changes in the means after this selection are small, and the difference between the two new means is still statistically significant.

TABLE III
CORNEAL RADIUS IN EYES WITH ACUTE GLAUCOMA AND IN NORMAL EYES
(Selected group with chamber depth between 1·5 and 2·1 mm.)

Eyes	Number	Average Corneal Radius (mm.)
Glaucomatous	76	7·50 ± 0·028
Normal	57	7·73 ± 0·037
Difference		0·23 ± 0·046

In 47 cases of uni-ocular acute glaucoma, the average difference between the corneal radius of the healthy eye and that of the diseased eye is very small and statistically insignificant (0·004 mm.). If the disease contributes to the reduction of the radius, a marked difference would be expected. Thus, it is probable that the radius is the same even before the disease and that the small radius as well as the shallow chamber is a predisposing factor in acute glaucoma.

Comment

The results indicate that in acute glaucoma the corneal radius is on an average about 4 per cent. less than in normal eyes. This reduction probably characterizes the structure of an eye predisposed to this condition. Earlier investigations indicate that a shallow anterior chamber is also common in eyes predisposed to this condition. The chamber depth is on an average 30 per cent. less than in normal eyes (Törnquist, 1956b). On account of the difference in reduction of these two measurable elements it seems as if the anatomical proportions are changed. However, a closer analysis will require further measurements, especially of the diameter and length of the eyeball and the size of the lens.

Summary

(1) The radius of curvature of the cornea in eyes with acute glaucoma is on an average 4 per cent. less than in normal eyes.

(2) The small radius seems to be a predisposing factor in the aetiology of the disease.

(3) The difference in the reduction of the corneal radius and that of the chamber depth indicates a disproportion in the structure of an eye predisposed to acute glaucoma.

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A PHOTOGRAPHIC METHOD OF MEASURING THE ANGLE OF SQUINT*

BY

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MEASUREMENT of the angle of deviation in squint is usually made either objectively or subjectively by means of the major amblyoscope. This instrument has the disadvantage that, although the fixation object is optically at infinity, the known proximity of the apparatus may stimulate convergence (see, for instance, Schapero and Levy, 1953). The readings vary from operator to operator, especially by the objective method, and may differ widely from the visual estimate made by a practised surgeon from observation of the corneal reflex.

An attempt has been made to avoid some of these difficulties by assessing the angle of squint by photographic means. This also provides a permanent record which may be compared with similar records obtained later. The method to be described, though more time-consuming than that using the synoptophore, requires a minimum of co-operation from the patients, in that they are simply required to fix a small light. It places on a quantitative basis the method employed in visual estimation of the angle by the position of the corneal reflex.

Apparatus

The apparatus consists of a fixed-focus camera employing a large aircraft camera lens of focal length 20″ and relative aperture F 6·3, supported on a rigid steel framework 30″ from the floor. Immediately in front of the film is a 2½″ pneumatic studio shutter, operated by a bulb which can be held in the operator's hand. The shutter mechanism is synchronized with an electronic flash of approximately 1/1500 sec. duration, situated immediately below and in front of the lens. A small fixation light can be moved along a tangent scale in a horizontal plane, at right angles to the principal axis of the system. In the present apparatus the length of this scale is limited by available space to a traverse of 20° to the right and 25° to the left. The subject is seated on an adjustable stool, with chin and forehead supported by a suitable rest which is rigidly attached to the camera in order to maintain correct focus. A numbering device is attached to the head-rest for convenience in identifying exposures. The distance between the subject's eyes and the camera lens is 325 cm., this being the distance at which the best focus was found experimentally. Kodak Panatomic-X 35 mm. film, processed with a fine-grain developer, gives satisfactory images for measurement.

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The processed film is examined by means of a travelling microscope fitted with an eyepiece containing a graticule divided into 100 divisions of 0·05 mm. each. These scale units are used in the calculation of results. The magnification is such that one division of the graticule scale is equivalent to 0·119 mm. at the subject's eye.

Method

The angle of squint may be assessed by measurement, on a photograph, of the movement of a single point on the eye, or of the relative movement between two individual points. After trial by means of superimposed exposures, the first method was found to be impracticable, principally because of the difficulty of eliminating head movement, particularly in children. The second method eliminates the effect of head movement, and is the method to be described. It will be considered first on the assumption that the eye has a fixed centre of rotation, situated on the optic axis. The effect of this assumption and possible resultant errors will be considered later.

Fig. 1 represents the cornea of an eye with fixation axis along SF and optic axis along SCP. The angle FSC then represents the angle γ of physiological optics. The lines LD, MB, which are perpendicular to SF, subtend angles ω_L and ω_M at the centre of curvature of the cornea C. The image of the fixation light will lie on the normal to the corneal surface, that is, at a point on the line CX, which may be considered parallel to SF provided the fixation light is sufficiently distant. This image, on a photograph taken from the position of the fixation light, will be displaced from the points L and M by distances corresponding to LD, MB respectively.

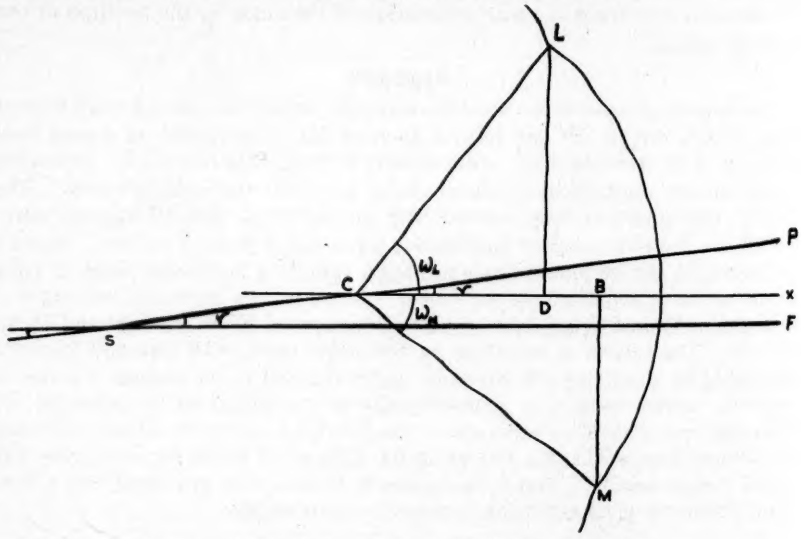

FIG. 1.—Schema of cornea of an eye in the primary position.

Fig. 2 shows the relationships when the eye has rotated about S through an angle of $\theta°$. The fixation axis is now along SF′, and the image of the original fixation light will lie on the line CX′, which again is parallel to SF for a distant light source. The displacements of the image from L and M will now be LD′ and MB′ respectively.

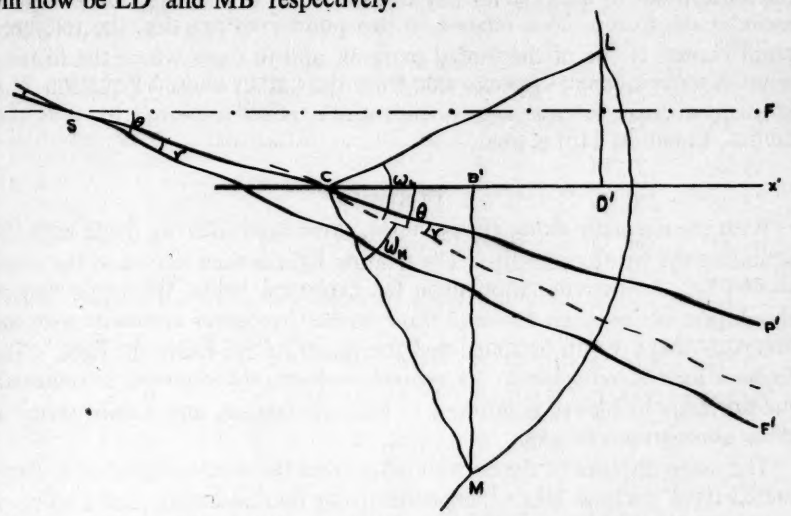

FIG. 2.—Schema of cornea of an eye deviated through an angle of $\theta°$.

Let LD or MB$=e$; CL or CM$=q$; LD′ or MB′$=x$.

The following trigonometrical relationships now hold:

For measurements involving point L,

$$e = q \sin \omega_L$$

and

$$x = q \sin (\omega_L - \theta)$$

whence

$$\tan \omega_L = \frac{e \sin \theta}{e \cos \theta - x} \quad \ldots\ldots \quad 1\,(a)$$

and

$$\sin (\omega_L - \theta) = \frac{x \sin \omega_L}{e} \quad \ldots\ldots \quad 2\,(a)$$

For measurements involving point M,

$$e = q \sin \omega_M$$

and

$$x = q \sin (\omega_M + \theta)$$

whence

$$\tan \omega_M = \frac{e \sin \theta}{x - e \cos \theta} \quad \ldots\ldots \quad 1\,(b)$$

and

$$\sin (\omega_M + \theta) = \frac{x \sin \omega_M}{e} \quad \ldots\ldots \quad 2\,(b)$$

The value of ω can be determined from Equation 1 by measuring e and x at a known value of θ, and it may be used in Equation 2 (a) or 2 (b) with a new

value of x to determine an unknown value of θ. The method is independent of the value of angle γ. It will be noted, however, that the values of ω_L and ω_M will differ owing to the angle γ and the asymmetry of the cornea. Care must be taken, therefore, always to use the value of ω relevant to the reference point in use, and to pay due attention to the direction of movement of the fixation axis relative to this point. In practice, the reference point chosen is one of the limbal margins, and in cases where the fixation point is moved to the opposite side from the limbus chosen Equation 2 (*a*) is used, whereas in cases where the fixation point is moved towards this limbus, Equation 2 (*b*) is used.

Procedure

With the normally-fixing eye occluded, three exposures are made with the squinting eye fixing centrally. The fixation light is then moved to the angle chosen for the determination of ω (as explained below the angle chosen should not be less than 15°) and three further exposures are made with the non-squinting eye still occluded and the squinting eye fixing the light. The fixation light is returned to its central position, the occluder is removed, the normally-fixing eye is allowed to take up fixation, and a third series of three photographs is taken.

The mean distance of the corneal reflex from the temporal limbus is determined from readings taken independently by two observers, and a value of ω is obtained from Equation 1, using the angular displacement of the fixation light as the value of θ, and the mean of three readings from the first two sets of exposures as values of e and x respectively. This value of ω is then substituted in Equation 2 (*a*) or 2 (*b*) together with the value of θ as above and the new value of x; in this case, x is the mean of the three readings comprising the third set of exposures.

Results

For Known Fixation Angle.—In order to assess the variations in ω from eye to eye, and with the fixation angle, measurements were made on four normal subjects and on three children with convergent squint. In the normal subjects, x was measured for four values of θ (5°, 10°, 15° and 20°) both to right and left and for both eyes. The resultant values of ω are shown in Table I (opposite). These values show a larger variation between 5° and 10° than between 15° and 20°.

In the three children, ω was determined for at least one angle other than the expected angle of squint. The results in Table II (opposite) show the variation in the value of ω and its effect on the value of the angle of squint.

Cases of Squint.—Fifteen children with convergent strabismus were examined on the occasion of admission to hospital for operation. Their ages ranged from 7–15 years, and the angles of squint without correction

TABLE I

VALUES OF ω OBTAINED FOR DIFFERENT ANGLES OF FIXATION IN NORMAL SUBJECTS

Subject No.	Eye	Fixation Point: Direction	Displacement 5°	10°	15°	20°
1	R	Right	52° 08′	46° 07′	45° 28′	45° 00′
	L		50° 12′	53° 23′	53° 33′	52° 04′
	R	Left	52° 05′	52° 16′	54° 37′	52° 05′
	L		53° 33′	46° 43′	43° 28′	46° 53′
2	R	Right	43° 16′	44° 59′	43° 40′	43° 51′
	L		54° 52′	52° 33′	53° 46′	51° 46′
	R	Left	51° 19′	50° 09′	53° 41′	51° 05′
	L		46° 28′	42° 13′	42° 00′	41° 35′
3	R	Right	45° 42′	45° 03′	38° 15′	38° 18′
	L		55° 27′	56° 11′	52° 34′	53° 36′
	R	Left	50° 32′	60° 28′	55° 28′	53° 18′
	L		44° 33′	46° 00′	38° 50′	38° 54′
4	R	Right	40° 06′	46° 52′	41° 20′	40° 12′
	L		48° 24′	58° 43′	53° 42′	56° 05′
	R	Left	63° 42′	56° 44′	52° 05′	53° 30′
	L		47° 36′	44° 04′	40° 10′	40° 36′

TABLE II

VALUES OF ω OBTAINED FOR DIFFERENT ANGLES OF FIXATION SHOWING EFFECT ON ESTIMATED ANGLE OF SQUINT

Subject No.		Fixation Angle used to Determine ω	ω	Calculated Value for Angle of Squint
1	With Glasses	5°	60° 53′	6° 05′
		15°	55° 45′	5° 07′
	Without Glasses	15°	60° 21′	18° 45′
		5°	60° 09′	18° 39′
2	No Glasses	20°	62° 02′	33° 10′
		15°	60° 16′	31° 56′
		10°	64° 07′	34° 39′
		5°	69° 18′	38° 33′
3	With Glasses	15°	55° 37′	15° 59′
		25°	53° 32′	15° 02′

of the refractive error ranged from 5°–45°. All the patients were being operated on for cosmetic reasons and none had binocular vision. The angle of squint was measured objectively on the synoptophore by the orthoptic department staff immediately before photography. If the patient wore glasses both synoptophore and photographic measurements were made with and without the child's own spectacles. It was found that the large diffuse reflections from the lenses did not interfere with the photographic method, as they were easily distinguished from the small, sharp corneal reflex. The results of this series are shown in Table III (opposite).

Discussion

Possible sources of error fall into two groups:

(1) Those due to theoretical assumptions regarding the optical constants of the eye;
(2) Those due to inaccuracies of measurement in practice.

The former may be listed as follows:

1 (*a*).—The centre of rotation may not be a fixed point in relation to the eye and may not lie on the optic axis.

Numerous attempts have been made to establish the position of a point about which the eye can be considered to rotate (see, for instance, Duke-Elder, 1938). According to Park and Park (1933) the maximum translatory movement of the centre of rotation in space amounts to about 1 mm.; Emsley (1946) considers that the centre of rotation may be taken as approximately a fixed point about 15 mm. back from the anterior surface of the cornea and displaced about 1·67 mm. to the nasal side of the primary line (fixation axis in the primary position of the eye). Whatever approximation is adopted, its position within the eye will vary between individuals and with the direction of fixation, but is sufficiently small to have no serious effect on the value of ω or θ. Any movement with reference to co-ordinates in space will apply to all parts of the eye and affects the angle of view of the cornea. At the distance employed in our apparatus this effect is negligible.

1 (*b*).—The source and the camera are situated at a finite distance from the eye, and incident rays are not parallel. At the distance of 325 cm. used, the departure from parallelism is negligible.

1 (*c*).—The value of the angle of squint obtained will be increased by approximately the amount of convergence at the operating distance. This is no disadvantage, provided it is not taken as a true measurement for fixation at infinity. The difference in any case is only about 0·5°.

1 (*d*).—The cornea is not truly spherical, as the corneal radius of curvature increases steadily towards the periphery, and the value of ω depends on the

TABLE III
ESTIMATED ANGLES OF DEVIATION IN FIFTEEN CASES OF CONVERGENT SQUINT

No	Refraction (if worn)	Diagnosis	Glasses	Angle on Synopto-phore	Photographic Measurement
1	—	Right amblyopia Right concomitant convergent squint		10°	18°
2	R +4·5 D sph.	Alternating squint	with	8°	13°
	L +4·0 D sph.		without	20°	22°
3	R +6·00 D sph.	Right concomitant convergent squint	with	10°	15°
	L +5·50 D sph.	Right amblyopia	without	20°	27°
4	R +8·0/ +1·0 × 90	Right concomitant convergent squint	with	15°	17°
	L +6·5/ +0·75 × 90	Right amblyopia	without	35°	29°
5	R +2·0 D sph.	Left concomitant convergent squint	with	5°	6°
	L +2·0 D sph.		without	18°	19°
6	—	Right concomitant convergent squint Right amblyopia		25°	33°
7	—	Left concomitant convergent squint Left amblyopia		40–45°	38°
8	—	Right concomitant convergent squint		8°	13°
9	R +3·75 D sph.	Left concomitant convergent squint	with	15°	16°
	L +2·75 D sph.	Left amblyopia	without	25°	29° varying to 11°*
10	R +6·25/ +0·5 × 90	Left concomitant convergent squint	with	8°	17°
	L +5·5 D sph.	Left amblyopia	without	30°	38°
11		Left concomitant convergent squint Left amblyopia		30°	36°
12	R +2·0/ +1·5 × 90	Left concomitant convergent squint	with	5°	6°
	L +2·0/ +1·5 × 90		without	18°	12°
13	—	Right concomitant convergent squint Right amblyopia		25°	25°
14	—	Right concomitant convergent squint Right amblyopia		40–45°	47°
15	—	Right concomitant convergent squint		10°	4°

* Noted to be variable before photographing

position of the centre of curvature for the zone in use. Unless, therefore, the reflex is formed by the almost spherical optical zone of the cornea, the value of ω will change as more peripheral parts of the cornea are used. This means that, unless the same zone is used for the determination of ω and θ, a false estimate of the angle of deviation will be obtained. The error is minimized by determining ω at an angle as near as possible to the expected angle of squint. As the optical zone is used for deviations of up to 15°, it is unnecessary, and as discussed below, undesirable, to use angles of less than 15° for determining ω, but, as the eye deviates beyond 15° and flatter peripheral zones form the image, an alteration in the value of ω may be expected, and it is then advisable to determine ω for an angle near to the expected angle of squint, which may be assessed visually before photographing.

2 (*a*) *Variations in* ω.—As noted above, values of ω show a larger variation between 5° and 10° than between 15° and 20°. This is due principally to errors in scale reading, which have a much greater effect where θ is small and the quantity $e \cos \theta - x$ is also small. In order to minimize such errors, it is advisable not to use angles of less than 15° for the determination of ω. At 5°, the error due to a misreading of the scale by one division alters the value of ω by about 8°, whereas at 10°, 15°, and 20° the corresponding figures are 4°, 2·5°, and 1·5° respectively. As would be expected, values of ω vary from subject to subject, and also to a much lesser extent between the right and left eyes of the same subject.

2 (*b*) *Variations between Synoptophore and Camera Measurements.*—Table III shows that there are considerable differences between the angles estimated objectively by the synoptophore and by the photographic method. This is in accord with the experience of some surgeons who have noted that on occasion the visual estimate obviously fails to agree with the synoptophore reading. It is not proposed to discuss these fully here, as it is intended to investigate a larger series of patients to confirm and elucidate these discrepancies. They are in part due to the experimental error in both synoptophore and camera measurements. In the photographic method the six readings which are averaged to obtain each value vary by an average of less than one scale division. A cumulative error of one scale division in each of the three values used in calculating a 20° squint will result in an error of 2·5°.

Fixation can be controlled to some extent by placing the operator near the patient so that the exposure is not made during a period when fixation is lost or unsteady. Difficulties in measurement arise chiefly in the identification of a clear reference point at the limbus, as this may extend over two to three scale divisions without any abrupt line of demarcation. As, however, all measurements are made in succession, it is possible with practice to measure from a corresponding point in this zone in each photograph of a

given patient. This is the cause of some of the variations in readings by two observers on the same photograph, and it is worth noting that in these cases every measurement on that subject tends to be assessed as larger by one observer. This to some extent nullifies the difference in individual readings.

Summary

A method of estimating the angular deviation of the eyes of subjects with lateral squints by measurement on photographs is described. Theoretical and practical sources of error are discussed.

We wish to express our gratitude to Mr. O. M. Duthie and Dr. A. Stanworth for allowing us to see their patients.

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Brit. J. Ophthal. (1957) **41**, 434.

CASE NOTES

UNILATERAL EXOPHTHALMOS RESULTING FROM SCLEROSIS OF THE SPHENOID BONE*

BY

J. W. E. CORY

Bury St. Edmunds, Suffolk

Case Report

A woman aged 53 was sent by her doctor to the West Suffolk General Hospital in July, 1955. She said that her right eye had become more prominent during the last year, but a snapshot taken 2 years previously suggested a prominence of the right eye at that time. She made no complaint of any symptoms referable to the exophthalmos. Her weight was constant and she preferred hot weather to cold. There was no past history of a serious illness except deafness resulting from measles 30 years previously. Her father was alive and well at the age of 80 and her mother had died at 81, having only suffered from some osteo-arthritis previous to her last illness. Two brothers and two sisters were alive and well. The patient was married and had a healthy son and daughter.

Examination.—She was a healthy-looking woman with 8 mm. proptosis of the right eye (Figs 1 and 2). Visual acuity (uncorrected) was 6/12 in each eye, with physiologically cupped discs and normal visual fields.

1

2

FIGS 1 and 2.—8-mm. proptosis of right eye.

X-ray examination of the skull showed a uniform sclerosis of bone in the right frontal and orbital region which was fairly well defined. The whole of the lesser and greater wing of the sphenoid and the lateral wall of the orbit and zygoma were sclerosed (Figs 3 and 4, opposite).

Serial *x* rays of the head in a gradually forward-tilting position to exclude the petrous temporal bone showed that both wings of the sphenoid were involved. *Lateral x rays* showed a normal sella turcica. Further *x* rays to cover the skeleton did not disclose any other bony lesion. The opaque left antrum would appear to be a simple infective condition while the sinus, ethmoids, and antrum of the affected side appeared to be normal.

The following pathological investigations revealed nothing abnormal:

Blood.—Red blood corpuscles 4,120,000; haemoglobin 93 per cent.; white blood corpuscles 7,800, polymorphs 62 per cent., lymphocytes 36 per cent., eosinophils 2 per cent.; erythrocyte sedimentation rate 19 mm./1 hr. Wassermann reaction and Kahn test negative. Alkaline phosphatase 5·6 units/100 ml.; total protein 6·6 g/100 ml., albumin 4·4, globulin 2·2, A/G ratio 2–1; serum cholesterol 130 mg./100 ml., blood phosphorus 2·6 mg./100 ml., serum calcium 10 mg./100 ml.

Urine.—No Bence-Jones protein.

* Received for publication February 20, 1957.

Lumbar Puncture. — Cerebro-spinal fluid clear and colourless, pressure 120 mm; Queckenstedt positive, protein 28 mg. per cent., cells none, no excess globulin, glucose normal.

FIG. 3.—Sclerosis of sphenoid extending to zygoma.

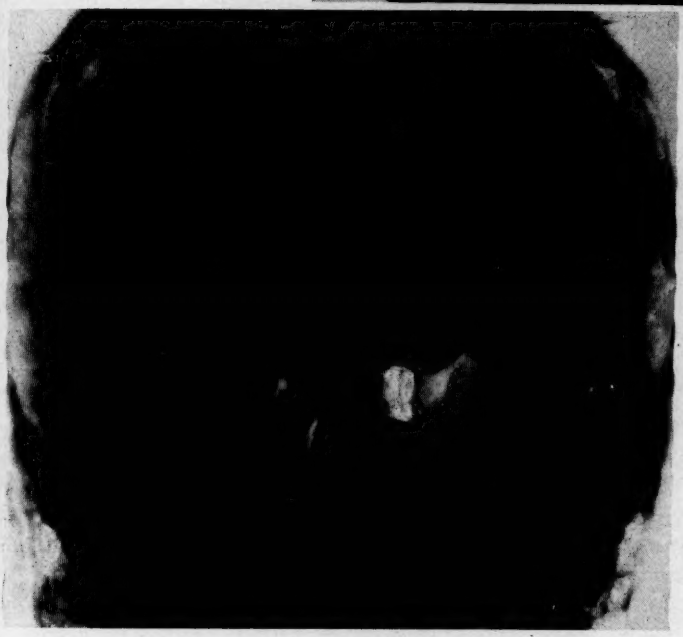

FIG. 4.—Antero-posterior view showing involvement of both wings of sphenoid.

Discussion

Duke-Elder (1952) discusses unilateral proptosis and gives a very full classification of causes; he goes on to discuss causes of the relatively rarer bilateral proptosis and gives a list of osteopathies. It would appear that a condition akin to osteitis fibrosa would be more likely to give rise to a

bilateral condition. Cory (1947) reported a case of fibrocystic disease of bone affecting the left orbit associated with glaucoma.

Sir Thomas Fairbank, who was good enough to see the films, writes:

> If it is leontiasis (fibrosis) it is quite unusually dense and uniformly dense in parts at least. I've not seen such intense uniform density in polyosteitic fibrous dysplasia.

Meningioma was considered until subsequent *x* rays showed that the outer table of the skull was mainly involved and that the sclerosis first noticed in the sphenoid extended to the zygoma and frontal bone. Oblique views showed the optic foramen and sphenoidal fissure to be of normal size and that in this position both tables were affected (Figs 4 and 5).

FIG. 5.—Oblique view, showing optic foramen and sphenoidal fissure of right side.

Benedict (1941) used the term hyperostoses to cover a variety of pathological lesions many of which arose from the soft structures, and said that thickening of the great wing of the sphenoid was frequently brought about by a meningioma spreading along the surface of the cranial vault. This may penetrate the bone and enter the orbit and cause exophthalmos, often with paralysis of ocular muscles.

In the case under discussion meningioma seemed to be ruled out by the involvement of the outer table, the spread to the zygoma, and the relatively unchanged condition of the patient after 18 months.

Harrison (1942) reported a case of osteoma of the orbit with resulting bilateral optic atrophy.

Newell (1948) reported a case of involvement of the right orbit with sphenoidal osteoma causing diplopia; the case was observed for 2 years, in which time no further symptoms appeared and there was no increase in the size of the tumour.

The earliest reports I have read are those of Hewett (1867), writing on exostosis of the skull. He appears to have travelled widely both in Great Britain and in Europe observing specimens in museums. No similar condition is described but he, along with other observers, notes the tendency of osteomata to occur near the suture lines, particularly those of the frontal bone.

Glenn (1950) discusses osteomata at length and describes circumscribed tumours, which may involve one or both tables of the skull. These may appear as diffuse tumours arising from the sphenoid or temporal bones or in the orbito-ethmoid or orbito-maxillary areas. The diffuse lesions produce tremendous thickening of the involved bones and are usually the type which give rise to most symptoms. Circumscribed osteomata are not difficult to recognize, as they appear as mould-like tumours from the surrounding bone or in the accessory air sinuses.

Summary

An unusual case of sclerosis of bone is discussed, which mainly affects the sphenoid bone, but extends to the zygoma and frontal bones. It would appear to belong to the osteomata, and, as Sir Thomas Fairbank writes, is too uniformly dense to belong to the leontiasis ossea or fibrocystic group of bone diseases. The condition would not appear to be rapidly progressive and no active treatment is considered advisable.

I am indebted to Dr. S. Mitra for the excellent radiographs, to Sir Thomas Fairbank for his help and criticism, and to Dr. H. M. Bird for the photographs.

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Brit. J. Ophthal. (1957) **41**, 438.

CASE NOTES

MULTIPLE MYELOMATOSIS AFFECTING THE ORBIT*

BY

DORIS ROSE AND CLIFFORD TAYLOR

Eastbourne

Case Report

A woman aged 56 came to the ophthalmic clinic on August 29, 1951, with marked non-pulsating proptosis of the left eye, first noticed a month previously and steadily increasing.

Examination.—The left eye was lower than the right and all movements were defective. Visual acuity in the left eye was 6/9. The retinal vessels were engorged. Some retinal haemorrhages were present. The right eye was normal, with visual acuity 6/6. The patient refused admission for investigation as she said she was otherwise perfectly well and had always been healthy. An *x*-ray examination was made by Dr. E. Owen Fox, who reported that the whole vault of the skull showed numerous rounded areas of rarefaction, the largest being in the frontal region on the left side. Similar areas were present in the lower jaw, clavicles, ribs, and mid-sternum. No changes were seen in the lumbar vertebrae.

On October 2, 1951, a general examination was made by Mr. Henry Wilson. Low back pain of some months' duration, which was relieved by lying down, and increasing constipation of 6 weeks' duration, were the only symptoms. There was no headache.

Progress.—On October 9, 1951, the patient was admitted as an emergency case. Extreme proptosis, now pulsating, with marked chemosis and some peri-orbital oedema, were present. A tarsorrhaphy was only just possible, the cornea already being hazy. There was tenderness over the lower spine and pelvis and slight tenderness in the right hypochondrium.

Laboratory Investigations.—Wassermann reaction and Kahn test negative.

Marked rouleaux prevented a red cell count being carried out. Hb 63 per cent. (Haldane), white cells 7,800 per cu. mm., differential count normal apart from the presence of a small number of plasma cells.

Erythrocyte sedimentation rate (Westergren) 150 mm./1 hr.

Blood urea, 139 mg. per cent., total serum protein 15 g. per cent., albumin 2 g., globulin 13 g., albumin/globulin ratio 1:6·5; serum calcium 12·4 mg. per cent., serum alkaline phosphatase 48 King Armstrong units.

Urine. Negative for Bence-Jones protein.

Sternal marrow showed the cells to be largely of the plasma series.

Diagnosis.—Multiple myelomatosis, in accordance with the *x*-ray reports and pathological findings.

Therapy.—A course of radiotherapy was given on October 25, 1951, which made the patient more comfortable.

Death occurred on November 19, 1951.

Necropsy Findings.—On opening the skull a tumour measuring 7 × 5 cm. was identified in the left frontal area, lying in the extradura between the frontal bone anteriorly and above, the dura behind and the orbital plate beneath. It was of firm consistency, being made up of dark red coagulum and pink-grey tumour tissue. It was firmly adherent to

* Received for publication February 27, 1957.

the dura but had not penetrated that membrane although it had partially flattened the left frontal area of the brain. Above the tumour, the inner table of the skull was eroded over a wide area, while below, the left supra-orbital plate was largely destroyed and a hole 4 × 3 cm. had been produced in which the tumour passed downwards into the orbital fat displacing the eyeball forwards (Figure). The cribriform plate on the left side was also eroded, the tumour having apparently arisen in the medullary cavity of the left frontal bone. The orbital ridge was of eggshell thickness and it easily crumbled under digital pressure. Myeloma deposits were also identified in other parts of the calvarium as well as in the sternum, clavicles, ribs, bodies of the thoracic and lumbar vertebrae, and in the long bones.

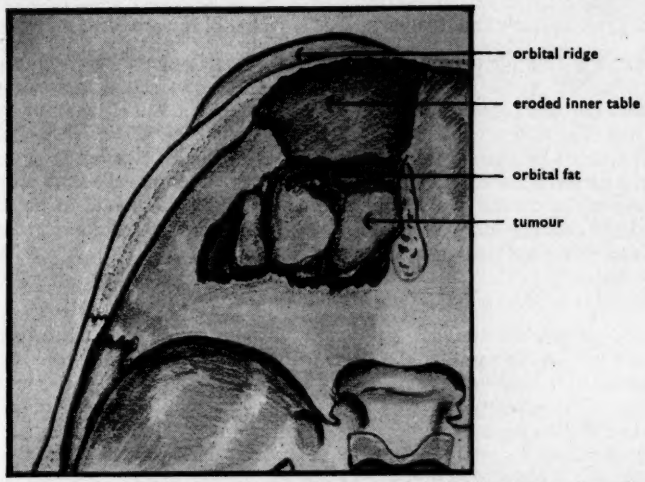

FIGURE.—Internal surface of left half of base of skull, showing erosion of orbital plate by myeloma.

Sections of the tissue taken from the orbital tumour, ribs, and sternum showed compact aggregates and broad sheets of cells of uniform structure, exhibiting the typical plasma-cell pattern with eccentrically-placed nuclei, abundant cytoplasm, and cartwheel-like disposition of the condensed nuclear chromatin. Recent haemorrhage was prominent in the tumour mass occupying the retro-orbital fat.

Comment

Physical well-being continued until the proptosis had been present for 2 months. It seems likely that a haemorrhage then occurred in the tumour mass, death supervening rapidly in 6 weeks. Although the tumour appeared to originate in the medullary cavity of the frontal bone, it was its penetration into the orbit which produced the proptosis, and this was the first symptom noted by the patient. Clarke (1953) states that myeloma affecting the orbit is very rare. This case is reported because it is thought that the necropsy findings may be of interest.

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Brit. J. Ophthal. (1957) **41**, 440.

COMPLETE RETROFLEXION OF THE IRIS WITH RETENTION OF NORMAL VISION*

BY

A. J. OGG

Salisbury

Case Report

A male aged 20 years was involved in a motor-bicycle collision in April, 1956. He was admitted on the same day to hospital in a confused state; he was unable to give a clear history, nor subsequently could he remember anything of the accident.

Examination.—The lids of the right eye were bruised, and the conjunctiva was considerably injected. In the lower third of the cornea was a small stellate rupture. The anterior chamber was present but shallow, and contained a 3 mm. hyphaema. No iris structure was visible. After 2 days, during which time both eyes were padded, the anterior chamber had reformed and the hyphaema had almost cleared; 18 days after the accident the patient's general condition was sufficiently good for a slit-lamp examination. The rupture of the cornea had soundly healed. The iris was found to be completely retroflexed and could be seen rolled back and firmly attached to the ciliary processes; the entire zonule was visible and was found to be undamaged. The lens was in no way injured or displaced. The angle of the anterior chamber was normal. No abnormality was found in the fundus, and the uncorrected visual acuity was 6/12.

Follow-up.—When last seen, nearly 9 months after the accident, the uncorrected visual acuity in the injured eye was 6/6, and the patient was able to read J.1 with ease. There was no evidence of intra-ocular activity or raised tension, and the lens remained completely clear. The patient's only symptom was one of slight photophobia in bright light.

At no time did the injured eye receive treatment with a mydriatic or miotic.

The Figure shows an enlarged slit-lamp photograph of a portion of the lens equator and the edge of the retroflexed iris.

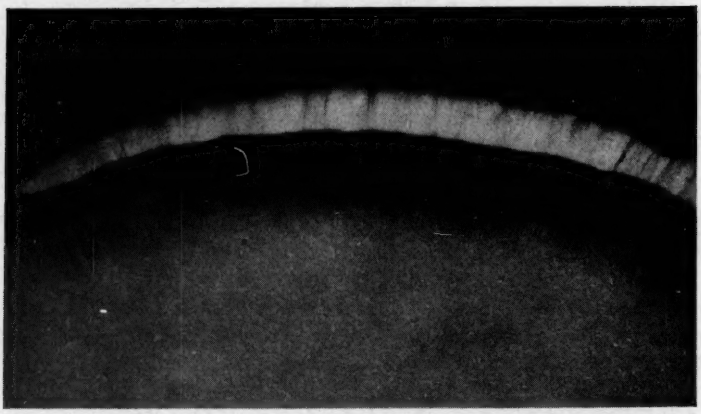

FIGURE.—Right eye, showing edge of retroflexed iris, two ciliary processes, and equator of the lens. Some equatorial and anterior zonular fibres are also shown.

* Received for publication February 20, 1957.

Discussion

Complete retroflexion of the iris is of rare occurrence. Parsons (1908), in a review of the recorded cases, found partial or complete rupture of the zonule an almost universal event, and the lens was usually dislocated. Duke-Elder (1954) described traumatic cataract and violent iridocyclitis as frequent accompaniments.

The interesting features of this case are that, despite a rupture of the cornea and complete iris retroflexion, the youthful zonule and lens are undamaged and the eye sees 6/6.

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Brit. J. Ophthal. (1957) **41**, 442.

TRANSIENT CYST FORMATION IN THE ANTERIOR CAPSULE OF THE LENS*

BY

A. HAGEDOORN

University Eye Hospital, Wilhelmina Gasthuis, Amsterdam

Case Report

A man aged 43, a tailor by trade, was referred to the hospital with a tentative diagnosis of glaucoma.

History.—He had suddenly seen clouds, never previously noticed, with his left eye, and when cycling in the evening he had seen haloes around lights.

These resembled the prodromal subjective phenomena of acute glaucoma, but glaucoma was excluded and the visual disturbances were explained by the slit-lamp findings.

Examination.—A delicate cyst was seen in the anterior capsule of the lens, with some tiny dots and ring-shaped opacities in its extremely thin walls. The Figure indicates the shape and size of the cyst, which had apparently developed by a splitting of the anterior capsule, or a local circumscribed detachment of the zonular lamella.

No separation of this size causing disturbing clinical symptoms could be found in the literature. The anatomy reminds one of the dehiscence of the zonular lamella found in glassworkers (Schnyder, 1926; Duke-Elder, 1954), but this cyst did not rupture, and the patient's work was not at all comparable with glassworking. Nor was there reason to consider the affection a presenile condition, since senile exfoliation starts in the zone behind the iris and not in the centre.

The visual acuity of the affected eye was reduced to 6/12 with +0·5 D sph., −1 D cyl.

The right eye was completely normal with normal visual acuity.

Follow-up.—On further examination 4 years later a well-marked but translucent macula capsulae lentis was found of about the same size as the cyst seen 4 years previously. Only a slight trace of fluid was left in the most inferior part of the cyst. Extremely small glistening dots and irregular lines were seen in this area by slit-lamp examination. By ordinary focal illumination, the central area of the capsule was slightly more opaque than the rest, a difference which might easily be overlooked in a routine examination. The visual acuity had improved to about normal, all subjective sensations had vanished, and the patient considered himself completely cured. This second examination, in which we found the subjective experiences of the patient confirmed by the objective findings, made it probable that the information he gave at the first examination had been reliable.

It must be concluded that a cyst developed in the anterior lens capsule or between the lens capsule and the zonule, giving rise to pronounced subjective complaints, which almost completely disappeared within 4 years.

* Received for publication January 29, 1957.

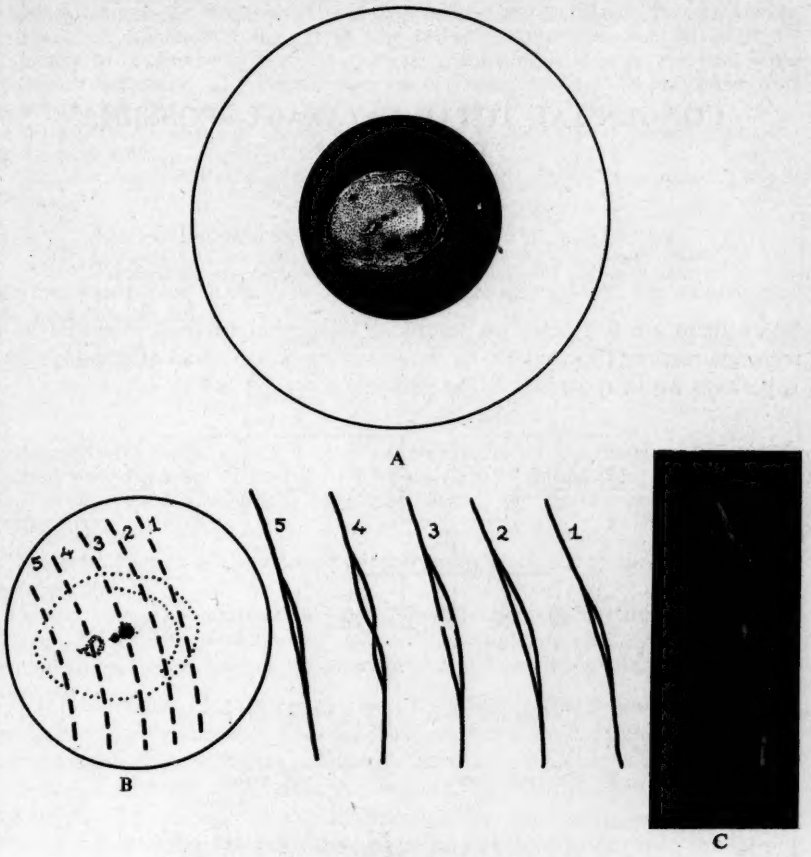

FIGURE.—Cyst of the anterior capsule of the lens.
(A) Front view, showing size and position of cyst
(B) Slit-lamp sections through the cyst
(C) Appearance of section No. 3.

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Brit. J. Ophthal. (1957) **41**, 444.

CONGENITAL TOTAL CATARACT—POSSIBLY RECESSIVE*

BY

RUBY JOSEPH

The Royal Eye Hospital and the Royal College of Surgeons of England

SINCE there are few cases on record of congenital cataract inherited in a recessive manner (Sorsby, 1951), the following report in an affected sibship is perhaps worth recording. The pedigree is set out in Fig. 1.

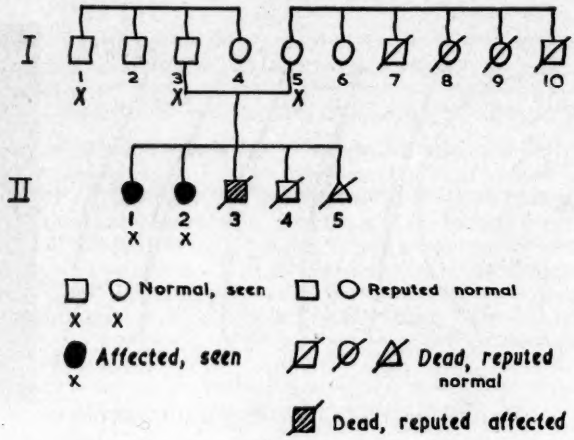

FIG. 1

Case Report

A girl aged 13 years (II, 1) had a history of having been born blind.

Examination.—She was well developed and intelligent. There were no signs of rickets. The eyes appeared slightly sunken and smaller than normal. Gross nystagmus was present. The corneae were clear, the anterior chambers of normal depth, and the pupils normal. The lens showed total cataract: no fundus view was possible.

Family History.—A younger sister was similarly affected. This child, aged 9 years (II, 2), was also found to be healthy and intelligent with no signs of rickets. The eyes appeared to be normal in size. Nystagmus was present. The corneae, anterior chambers, and

* Received for publication January 28, 1957.

pupils were normal. The lenses showed total cataract and no fundus view was possible.

Apart from a younger brother (II, 3), who died at the age of 1 year and was affected—according to the mother's statement—, there were no other affected members in the sibship or ascendants. The parents were not consanguineous nor did they come from neighbouring areas.

In the personal history of the mother there were no suggestion of rubella during any of the pregnancies.

The visual acuity of the father of the affected children (I, 3), who was aged 35, was as follows:

Right eye: unaided 6/60; with −3·5 D sph., −1 D cyl., axis 180°, 6/9.
Left eye: unaided 6/60; with −2·5 D sph., −1·5 D cyl. axis 180°, 6/6.

His eyes were normal in size. No lens changes were detected with the slit-lamp, and the fundi were normal.

The mother (I, 5), who was aged 30 years, was highly myopic; the visual acuity was as follows:

Right eye: with −12 D sph., 6/18.
Left eye: with −12 D sph., 6/18.

Her eyes were normal in size. There was no evidence of lens changes. The fundus showed typical changes of myopia. The discs were large and pale and there were large areas of choroidal atrophy all around them. The maculae showed dark pigmented areas.

The grandparents of the affected children were dead, but were reputed to have been normal.

It was possible to examine only one other member of the parent's generation (I, 1), and his eyes were normal. (Visual acuity 6/6 in each eye, emmetropic, normal globe, fundus normal, no anomalies of the lens visible with the slit-lamp.)

The occurrence of cataract in two and possibly three sibs—the cataract being identical in the two observed sibs—makes it unlikely that an environmental factor came into play. Though there is no evidence of consanguinity, recessive autosomal inheritance is likely and could fit in with similar cases recorded. The alternative explanation, that in this family the cataract was inherited in an irregularly dominant manner, finds no support in the family history or in the literature.

I wish to thank Professor Arnold Sorsby for his help and encouragement in the preparation of this paper.

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Brit. J. Ophthal. (1957) **41**, 446.

ANTERIOR DISLOCATION OF THE LENS IN MARFAN'S SYNDROME*

BY

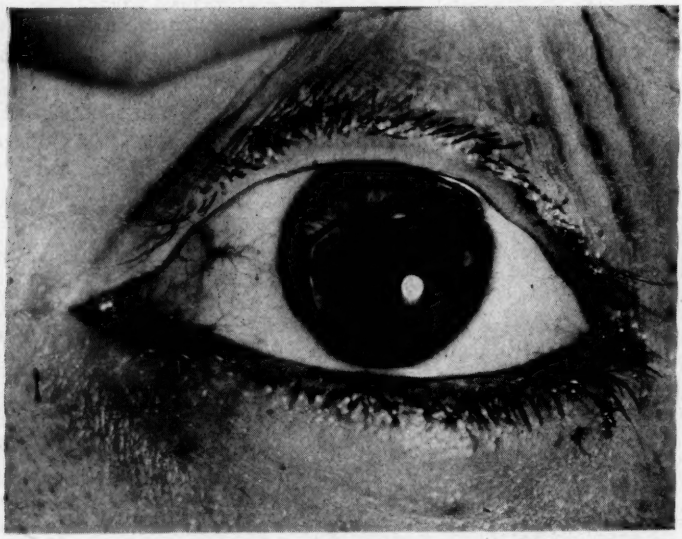
D. P. CHOYCE

Southend General Hospital, Essex

Case Report

A girl aged 14, coming from a family several members of which suffer from Marfan's syndrome, has many of the usual components of the syndrome, including a high arched palate, arachnodactyly, and microphakia, with congenital dislocation of the lenses. The condition was recognized when she was about 8 years old, since when she has been wearing an aphakic correction (+10 D sph. right and left) which normally gives her a visual acuity of 6/6 in both eyes.

On November 23, 1956, she bent down to pick something off the schoolroom floor, and when she got up found that the sight of the right eye was blurred. When she was seen later that day the right lens was dislocated forward into the anterior chamber, where it could be made to float freely about by altering her posture. She was conscious of a faint irritation of the eye, but no pain, the ocular tension being normal. The lens was perfectly clear and irregularly shaped, as shown by the Figure. The pupil behind it was miotic. The visual acuity in the right eye was reduced to counting fingers.



* Received for publication February 5, 1957.

Management of the Case.—Mindful of reports of cases in which the lenses can be transferred without much difficulty from anterior to posterior chamber, as described by Das Gupta and Basu (1955), it was decided to try to persuade the dislocated lens to return into the posterior chamber whence it came. The pupil was dilated with homatropine and, by positioning the patient on the operating table, the lens was manœuvred over the pupil, and pressure made on it through the overlying cornea. Unfortunately, instead of passing freely into the posterior chamber, it became gripped by the iris sphincter, with the upper pole behind the iris and the lower pole still in the anterior chamber. No amount of stimulation, either pharmacological or mechanical, could persuade the iris to release its hold.

Within 12 hours the patient was complaining of pain, and the eye was in a state of acute congestive glaucoma. The ocular tension had risen to 80–90 mm. Hg (Schiötz), and the cornea was oedematous. 500 mg. of Diamox, followed by 250 mg. 6-hrly, succeeded in reducing the pressure to 50/55 mm. Hg the next day, but the patient was still in pain and the cornea still oedematous. Operation was therefore indicated, albeit under conditions very much less propitious than if it had been undertaken when the lens was floating freely in the anterior chamber.

Anaesthesia.—In order to obtain maximum relaxation, the operation was performed under general anaesthesia.

First, an intravenous infusion was set up consisting of Pethidine, Phenergan, and Largactil. Anaesthesia was induced with intravenous thiopentone. Intubation was carried out under intravenous scoline, and anaesthesia was maintained with endotracheal nitrous oxide and oxygen, supplemented by a continuation of the above intravenous infusion. A further dose of thiopentone was given before surgery was begun.

Operation.—After the eye had been fixed with a superior rectus stitch, a small incision was made at the superior limbus with a von Graefe knife from 10 o'clock to 2 o'clock. In the middle of inserting the first cornea-scleral suture, the iris suddenly released the lens which shot out of the eye, and the section bulged ominously. In order to close the section securely, it was necessary to perform a wide complete iridectomy; fortunately, no vitreous was lost, though obviously its anterior surface was greatly disturbed.

Result.—The post-operative course was prolonged owing to considerable corneal oedema. However, good healing eventually took place, and 3 months after the operation the patient's vision is once again 6/6 with her aphakic correction. She complains somewhat of the additional light let in by the superior iris coloboma.

The dimensions of the lens were 7·5 × 6·5 × 4 mm., well illustrating the microphakia which is usually part of the syndrome.

Discussion

It cannot be assumed that, because a lens dislocates readily into the anterior chamber, it will prove equally easy to replace it in the posterior chamber. The rapidity with which acute congestive glaucoma developed once the lens became trapped by the iris was very striking. The danger to the eye is probably less if lens extraction is undertaken as soon as anterior dislocation occurs without attempting to replace the lens in the posterior chamber. Although, to date, aphakic detachment has not occurred in the operated eye, we feel that the danger of this happening has been made

greater by the comparatively clumsy operative procedure to which the patient was subjected.

Summary

(1) A case of spontaneous anterior dislocation of the lens in Marfan's syndrome is described. An attempt to replace the lens in the posterior chamber led to the onset of acute congestive glaucoma.

(2) Our experience suggests that, when anterior dislocation occurs, the right procedure is to remove the lens without delay.

I am indebted to Dr. C. H. Pryor for describing the anaesthetic which he gave, and to Mr. J. Wood for the illustration.

REFERENCE

DAS GUPTA, B. K., and BASU, R. K. (1955). *British Journal of Ophthalmology*, **39**, 566.

BOOK REVIEW

Neurology of the Ocular Muscles. By D. G. COGAN. 2nd edition, 1956. Pp. 296, 86 figs, Bibl. Blackwell, London. (63*s*.)

The second edition of "Neurology of the Ocular Muscles" has been enlarged to 296 pages and, apart from new work which has been added, particularly concerning the cerebellum, there have been some changes in emphasis. Thus, the myopathies as they affect the extra-ocular muscles are described in greater detail, and internuclear ophthalmoplegia receives more attention as important evidence of multiple sclerosis when bilateral, and of vascular disease when unilateral. Skew deviation and the difficulties of its interpretation are discussed.

The text has all the qualities of authority drawn from practical experience, although every page shows evidence of a deep knowledge of the literature. There are no less than 1,141 references, which take up 54 pages of the book, and a further 11 pages are given over to an excellent index. The subject matter is written in a gentle, pleasing style, beginning with the elements of gross anatomy which we all know so well, and gradually increasing in complexity as the author reaches the supranuclear connexions of the ocular motor system, and passes on to the real difficulties of nystagmus and its associated syndromes. It is a long time since the reviewer has gained so much pleasure in reading a text-book of medicine, and enjoyed throughout the lucidity of language and expression. The book can be highly recommended for senior students and for all practising ophthalmologists as a delight in store, and as a practical guide in difficult clinical problems.